

AVA AUTUMN MEETING 2019PROCEEDINGS BOOK.....

PRE-CONGRESS



AVA

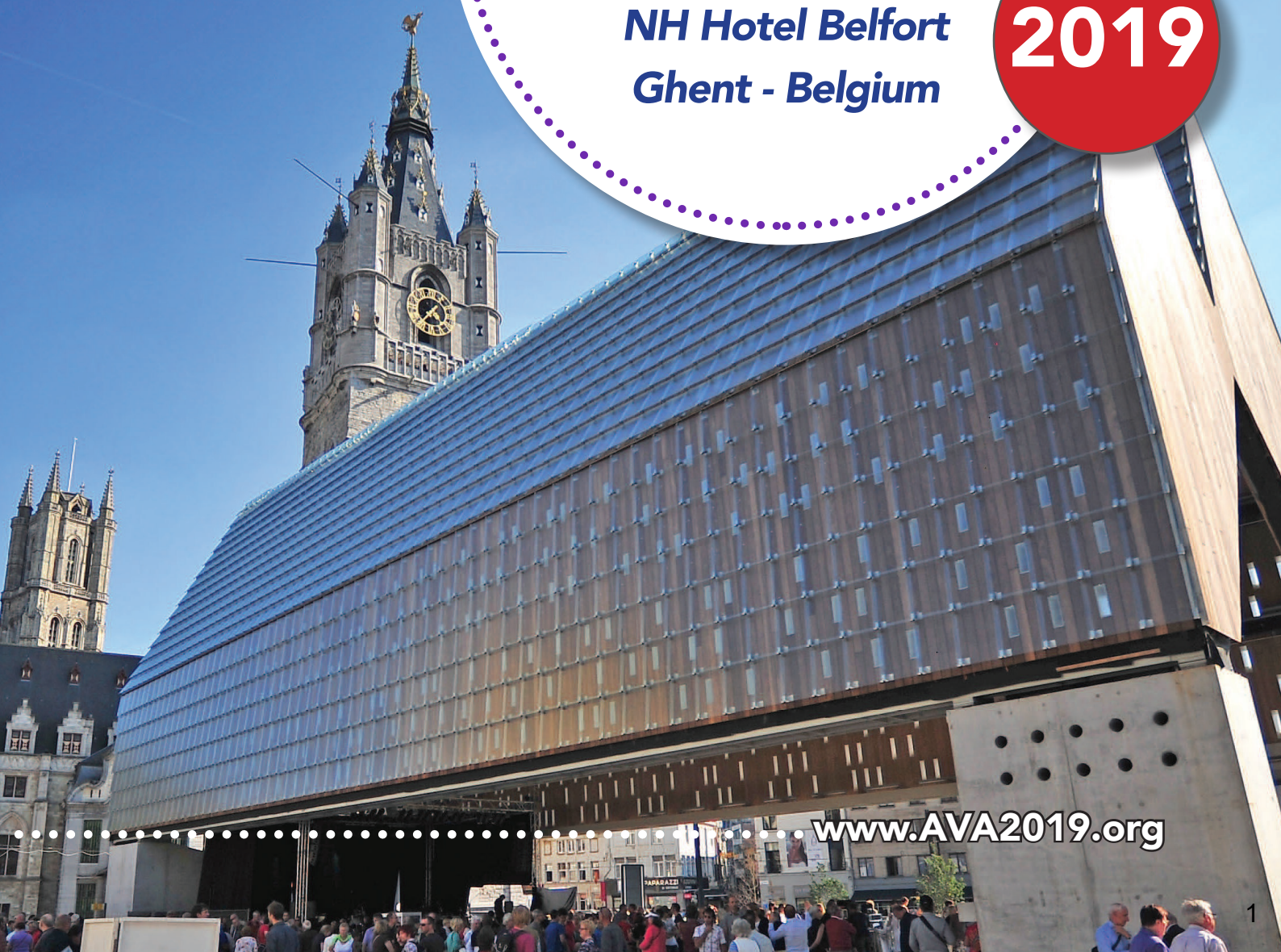
**Association of Veterinary
Anaesthetists**

11-13 September 2019

**NH Hotel Belfort
Ghent - Belgium**

2019

www.AVA2019.org



Proceedings Pre-congress Day

AVA Autumn meeting

Ghent, Belgium

11 - 13 September 2019

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Programme

Wednesday 11th September (pre-congress day)

9.00 – 10.15 Surviving sepsis in small animals (K. Gommeren)

10.15 – 10.45 Break & exhibition

10.45 – 11.30 Fluid therapy in small animals (K. Gommeren)

11.30 – 12.15 Acute kidney injury in small animals (S. Cortellini)

12.15 – 13.15 Lunch

13.15 – 14.30 Ventilation in the ICU in small animals (S. Cortellini)

14.30 – 15.15 Fluid therapy and resuscitation in foals (E. Paulussen)

15.15 – 15.45 Break & exhibition

15.45 – 16.30 Sepsis and perinatal infections in foals (A. Dufourni)

16.30 – 17.30 Fluid therapy and sepsis in ruminants (B. Pardon)

Our speakers

	Stefano Cortellini graduated at the University of Perugia in 2006 and after two years in private practice in Rome, he then performed a rotating internship at the Animal Health Trust. He became American Specialist in Emergency and Critical Care in 2014 following a residency in ECC at the RVC and is also European and RCVS Recognised Specialist in ECC. Stefano is co-director of the Renal Replacement service and loves every aspect of critical care but is particularly focused in biomarkers for AKI, extracorporeal therapies, sepsis and coagulation abnormalities. Stefano is chair of Scientific Committee of the European Veterinary Emergency and Critical Care society and is Member-at-Large of the European Veterinary Emergency and Critical Care College.
	Ellen Paulussen completed her studies as a veterinarian at Ghent University in 2013. She then followed an equine rotating internship at the Surgery department. Immediately afterwards, Ellen started as a resident at ECEIM (European College of Equine Internal Medicine) under the supervision of Gunther van Loon at the department of Large Animal Internal Medicine of Ghent University. In 2018 Ellen worked part-time at the Lingehoeve veterinary medicine in the Netherlands and part-time as a practical assistant at the faculty of veterinary medicine at the department of internal medicine. Currently Ellen is doing a PhD in equine cardiology in Ghent.
	2005 – 2012: Bachelor and Master of Veterinary Medicine – Ghent University - Belgium 2012 – 2014: Equine Veterinary Surgeon in Ambulatory Practice 2014 – 2015: Equine Rotating Internship Ghent University, Option Internal Medicine October 2015 – March 2019: European College of Equine Internal Medicine Residency at Ghent University – Department of Large Animal Internal Medicine Residency completed - Credentials accepted – Waiting to sit the exam February 2016: Certificate in laboratory animal science March 2019 – present: PhD in Equine Cardiology at the Department of Large Animal Internal Medicine, Ghent University
	Kris Gommeren graduated in 2002 at Ghent University, where he performed an internship and a residency in internal medicine. He became a diplomate in internal medicine in 2009, and briefly worked in a private referral practice, before moving to Liège University, where he is in charge of the ECC-service. He obtained his PhD on the effects of systemic inflammation on the cardiovascular system. In 2017 he became diplomate in emergency and critical care. Kris is actively involved in the European Society of Emergency and Critical Care (EVECCS), of which he currently is past-president. He is consultant for an international veterinary company, working on the development of emergency and critical care facilities and the training of personnel. His main fields of interest are point of care ultrasound, the cardiovascular system, fluid therapy and the assessment of volume status.

9.00 – 10.15

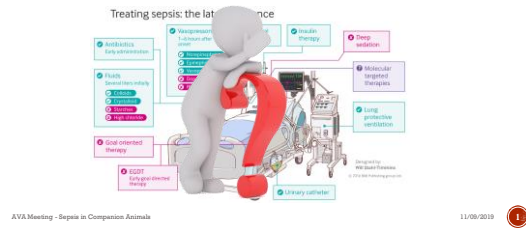
Surviving sepsis in small animals

(K. Gommeren)



SURVIVING SEPSIS IN SMALL ANIMALS

K. Gommeren DVM, MSc, PhD, DipECVIM-CA, DipECVECC



KEY FACT SEPSIS HUMANS ARE ANIMALS



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Surviving Sepsis Campaign

ABOUT SSC | GUIDELINES | HOUR-1 BUNDLE | RESOURCES | IMPLEMENT/IMPROVE | CONTACT

History

Inception 2002

Original Stated Goal of Campaign

To reduce mortality from sepsis by 25% via a 7-point agenda including:

- Building awareness of sepsis
- Improving diagnosis
- Increasing the use of appropriate treatment
- Educating healthcare professionals
- Improving post-ICU care
- Developing guidelines of care
- Implementing a performance improvement program

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doi:10.1016/j.sems.2019.05.001

Surviving Sepsis Campaign guidelines for management of severe sepsis and septic shock.

Defensori R, Carlet JM, Meiss EJ, Gerlach H, Calzavara J, Cohen J, Gao S, Gendreau J, Kahn D, Marshall JC, Parker MM, Ramsay G, Zimmerman AJ, Vincent JL, Levy MM. *Surviving Sepsis Campaign: Guidelines for the Management of Severe Sepsis and Septic Shock*.

Abstract

OBJECTIVE: In 2003, critical care and infectious disease experts representing 11 international organizations developed management guidelines for severe sepsis and septic shock that would be of practical use for the bedside clinician, under the auspices of the Surviving Sepsis Campaign, an international effort to increase awareness and improve outcome in severe sepsis.

RESULTS: Key recommendations, listed by category and not by hierarchy, include early goal-directed resuscitation of the septic patient during the first 6 hrs after recognition; appropriate diagnostic studies to ascertain causative organisms before starting antibiotics; early administration of broad-spectrum antibiotic therapy; reassessment of antibiotic therapy with microbiology and clinical data to narrow coverage, when appropriate; a usual 7-10 days of antibiotic therapy guided by clinical response; source control with attention to the method that balances risks and benefits; equivalence of crystalloid and colloid resuscitation; aggressive fluid challenge to restore mean circulating filling pressure; vasopressor preference for norepinephrine and dopamine; cautious use of vasopressin pending further studies; avoiding low-dose dopamine administration for renal protection; consideration of dobutamine inotropic therapy in some clinical situations; avoidance of supranormal oxygen delivery as a goal of therapy; stress-dose steroid therapy for septic shock; use of recombinant activated protein C in patients with severe sepsis and high risk for death, with resolution of tissue hypoperfusion and in the absence of coronary artery disease or acute hemorrhage, targeting a hemoglobin of 7-9 g/dL; appropriate use of fresh frozen plasma and platelets; a low tidal volume and limitation of inspiratory plateau pressure strategy for acute lung injury and acute respiratory distress syndrome; application of a minimal amount of positive end-expiratory pressure in acute lung injury/acute respiratory distress syndrome; a semirecumbent bed position unless contraindicated; protocols for warming and sedation/analgesia, using either intermittent bolus sedation or continuous infusion sedation with daily interruptions/lightening; avoidance of neuromuscular blockers, if at all possible; maintenance of blood glucose <150 mg/dL after initial stabilization; equivalence of continuous veno-venous hemofiltration and intermittent hemodialysis; lack of utility of bicarbonate use for pH > or < 7.35; use of deep vein thrombosis/stress ulcer prophylaxis; and consideration of limitation of support where appropriate. **Pediatric:**

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SURVIVING SEPSIS CAMPAIGN 2004-2008

Special Article

Surviving Sepsis Campaign: International guidelines for management of severe sepsis and septic shock: 2008

R. Phillip Dellinger, MD; Mitchell M. Levy, MD; Jean M. Carlet, MD; Julian Blein, MD; Margaret M. Parker, MD; Roman Jaeschke, MD; Konrad Reinhart, MD; Derek C. Angus, MD, MPH; Christian Brun-Buisson, MD; Richard Beale, MD; Thierry Calandra, MD, PhD; Jean-François Dohndau, MD; Hernali Gerlach, MD; Maureen Harvey, RN; John J. Marik, MD; John Marshall, MD; Marco Ranieri, MD; Graham Ramsay, MD; Jonathan Sevransky, MD; B. Taylor Thompson, MD; Sean Townsend, MD; Jeffrey S. Vender, MD; Janice L. Zimmerman, MD; Jean-Louis Vincent, MD, PhD; for the International Surviving Sepsis Campaign Guidelines Committee

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EFFECTS OF THE 2008 GUIDELINES

Original Research

Epidemiology and Changes in Mortality of Sepsis After the Implementation of Surviving Sepsis Campaign Guidelines

Rubén Herrán-Monge, MD¹, Arturo Muriel-Bombin, MD¹, Marta M. García-García, MD, PhD¹, Pedro A. Morino-García, MD¹, Miguel Martínez-Barrón, MD², David Andújar, MD, PhD³, Juan Carlos Ballesteros, MD⁴, Ana María Domínguez-Berrot, MD⁴, Susana Moradillo-González, MD⁴, Santiago Macías, MD⁴, Braulio Álvarez-Martínez, MD⁵, M. José Fernández-Cabrera, MD⁶, Concepción Tarancón, MD¹⁰, Jesús Blanco, MD, PhD^{1,11}; on behalf of the Spanish Sepsis Society (SESCS)

Journal of Intensive Care Medicine 2019 34(10):1071-1077. © The Author(s) 2019. Reprints and permissions: sagepub.com/journalsPermissions.nav DOI: 10.1177/1071198119851194 jicm.sagepub.com/home/jicm

Mortality 53 to 37%...

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EFFECTS OF THE 2008 GUIDELINES

Intensive Care Med (2018) 36:222–231
DOI 10.1007/s00135-018-0599-7

ORIGINAL

Mitchell M. Levy
R. Phillip Dellinger
Sean R. Townsend
Walter T. Linde-Zwirble
John C. Marshall
Julian Bone
Christina Schorr
Antonio Artigas
Graham Ramsay
Richard Beale
Margaret M. Parker
Horwig Gerlach
Konrad Reinhart
Elizavir Silva
Maureen Harvey
Susan Regan
Derek C. Angus

The Surviving Sepsis Campaign: results of an international guideline-based performance improvement program targeting severe sepsis

Mortality 37 to 30%...

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Surviving Sepsis Campaign: International Guidelines for Management of Severe Sepsis and Septic Shock: 2012

R. Phillip Dellinger, MD¹; Mitchell M. Levy, MD²; Andrew Rhodes, MB BS³; Djillali Annane, MD⁴; Horwig Gerlach, MD, PhD⁵; Steven M. Opal, MD⁶; Jonathan E. Sevransky, MD⁷; Charles L. Sprung, MD⁸; Joe S. Douglas, MD⁹; Roman Jaeschke, MD¹⁰; Tibiny M. Osborn, MD, MPH¹¹; Mark E. Nimmally, MD¹²; Sean E. Townsend, MD¹³; Konrad Reinhart, MD¹⁴; Ruth M. Kleinpell, PhD, RN-CP¹⁵; Derek C. Angus, MD, MPH¹⁶; Clifford S. Deutschman, MD, MS¹⁷; Flavia R. Machado, MD, PhD¹⁸; Gordon D. Rubenfeld, MD¹⁹; Steven A. Webb, MB BS, PhD²⁰; Richard J. Beale, MB BS²¹; Jean-Louis Vincent, MD, PhD²²; Rui Moreno, MD, PhD²³; and the Surviving Sepsis Campaign Guidelines Committee including the Pediatric Subgroup¹

- Emphasis on avoiding steroids
- Activated Protein C disappeared
- Colloids disappeared and albumin appeared
- Dynamic rather than static volume assessment
- Norepi 1st choice, avoid dopamine

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Format: Abstract +

Send to +

Clin Exp Med. 1999 Aug 23(8):1400-4.

Corticosteroid treatment for sepsis: a critical appraisal and meta-analysis of the literature.

GOUDAS L, GOUDAS C, BELLIS E, BARNES D, GOUDAS L, KARAKIS M, FANIKOLA S.

© Author information

Abstract

OBJECTIVE: To determine the effect of corticosteroid therapy on morbidity and mortality in patients with sepsis.

DATA SOURCE: We searched for published and unpublished research using MEDLINE, EMBASE, and the Science Citation Index, manual searching of Index Medicus, citation review of relevant primary and review articles, personal files, and contact with primary investigators.

STUDY SELECTION: From a pool of 124 potentially relevant articles, duplicate independent review identified nine relevant, randomized, controlled trials of corticosteroid therapy in sepsis and septic shock among critically ill adults.

DATA EXTRACTION: In duplicate, independently, we abstracted key data on population, intervention, outcome, and methodologic quality of the randomized controlled trials.

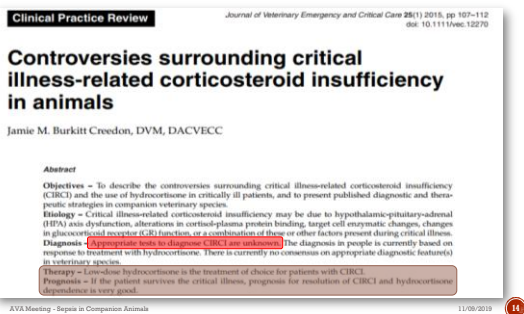
DATA SYNTHESIS: Corticosteroids appear to increase mortality in patients with overwhelming infection (relative risk 1.13, 95% confidence interval 0.99 to 1.29), and have no beneficial effect in the subgroup of patients with septic shock (relative risk 1.07, 95% confidence interval 0.91 to 1.26). Studies with the highest methodologic quality scores also suggest a trend toward increased mortality overall (relative risk 1.10, 95% confidence interval 0.94 to 1.29). A similar trend was observed for patients with septic shock (relative risk 1.12, 95% confidence interval 0.95 to 1.32). No difference in secondary infection rates was demonstrated in corticosteroid-treated patients with sepsis or septic shock. However, there was a trend toward increased mortality from secondary infections in patients receiving corticosteroids (relative risk 1.70, 95% confidence interval 0.70 to 4.12). The occurrence rate of gastrointestinal bleeding was increased slightly in the treatment group (relative risk 1.17, 95% confidence interval 0.79 to 1.73).

CONCLUSIONS: Current evidence provides no support for the use of corticosteroids in patients with sepsis or septic shock, and suggests that their use may be harmful. These trials underscore the need for future methodologically rigorous trials evaluating new immune-modulating therapies in well-defined critically ill patients with overwhelming infection.

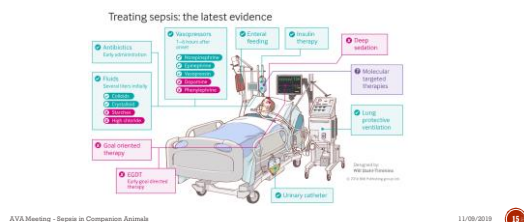
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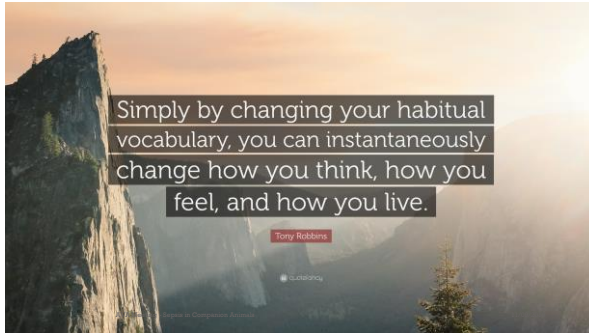
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SURVIVING SEPSIS CAMPAIGN 2016





SIRS ≠ SEPSIS

EMPHASIS ON LIFE-THREATENING RATHER THAN INFLAMMATORY

- Clinical SIRS diagnosis (*Hauptman et al.*)
 - Hypo- or hyperthermia <38,0/>39,2°C
 - Tachycardia >120beats/min
 - Tachypnea >20breaths/min
 - Leukocytosis or leukopenia <6000/>16000x10⁹/μL
 - Band neutrophils >3%
- Screening via qSOFA (>2/3)
 - Mentation GCS<15
 - Blood pressure SAP<100mmHg
 - Respiration RR>22bpm
 - Doesn't define sepsis, **indicates** high risk patients



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ORIGINAL ARTICLE

Prognostic accuracy of SIRS criteria, qSOFA score and GYM score for 30-day-mortality in older non-severely dependent infected patients attended in the emergency department

J. González del Castillo^{1,2}, A. Julian-Ruiz³, F. González-Martínez⁴, J. Álvarez-Manzanera⁵, P. Piliers⁶, C. Navarro-Bustos⁷, M. Martínez-Oveta de Zarate⁸, F. López-Roca⁹, M. Delballe Fernández¹⁰, J. Gonsano-Del Rio¹¹, E. J. García-Lambertucci¹², E. J. Martín-Sánchez^{1,2}, representing the Infection Disease Group of the Spanish Emergency Medicine Society (see addendum)

AUC

- qSOFA 0.69 (95% CI 0.61–0.76; p < 0.001)
- SIRS 0.65 (95% CI 0.59–0.72; p < 0.001)

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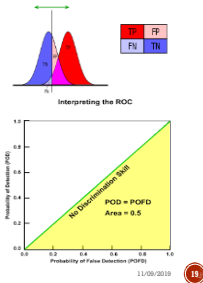


SIRS VS QSOFA

- SIRS criteria ≥ 2
 - sensitivity 68% (95% CI 53.1–75.9)
 - specificity 49% (95% CI 46.0–52.3)
- qSOFA score ≥ 2
 - sensitivity 28% (95% CI 18.2–39.8)
 - specificity 94% (95% CI 91.9–95.1)

Predict 30-day mortality
 SIRS ≥ 2 moderate Sens & Spec
 qSOFA ≥ 2 poor Sens & high Spec

- Lactate debated, but not agreed...



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SURVIVING SEPSIS CAMPAIGN 2016

Paediatric RED FLAGS... THINK SEPSIS!

The forecast upon Type Hospital: **Unpredictable**

Suspected or proven infection AND has 1 of the following:

- Core temperature $>38.5^{\circ}\text{C}$
- Inappropriate tachycardia (see HR to chart)
- Increased respiratory rate
- Altered mental state (i.e., inappetence, irritability, lethargy, floppiness)
- prolonged capillary refill (prolonged skin perfusion)

Have a lower threshold of suspicion for patient younger than 2 months, chronic disease, recent surgery, immunosuppressed

Suspect sepsis. Say sepsis. Save someone's life today!

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SEPSIS 3.0 EMPHASIS ON LIFE-THREATENING RATHER THAN INFLAMMATORY

- Sepsis now was severe sepsis
 - Implied organ involvement
- Mortality increases with organ dysfunction
 - SOFA (= sequential organ failure assessment) score >2
 - Neurologic
 - Hepatic
 - Renal
 - Coagulation
 - Respiratory
 - Cardiac

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SEPSIS 3.0

EMPHASIS ON LIFE-THREATENING RATHER THAN INFLAMMATORY

- Septic shock
 - Increased likelihood of death
 - **Despite adequate volume resuscitation**
 - MAP <65mmHg
 - Lactate > 2,0mmol/L

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DISEASE ENTITY $\neq$ EFFECT ON BODY

Septic Peritonitis

- Microbial contamination of the peritoneum
- Inflammation
 - Ascites
 - Fever
 - GI-symptoms



Septic Shock (Sepsis-3.0)

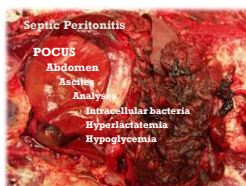
- Organ dysfunction (SOFA >2)
- Decreased perfusion
 - Circulatory
 - Cellular/metabolic problems
 - Associated with mortality

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SEPTIC PERITONITIS $\neq$ SEPTIC SHOCK



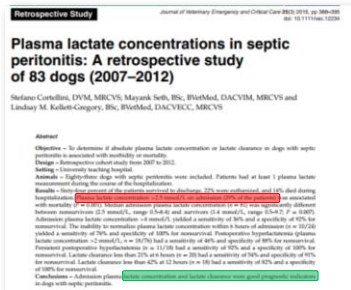
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Septic Shock

- Hypotension
 - MAP <65mmHg
 - SAP <80-90mmHg
- Hyperlactatemia
 - >2,0mmol/L
- Insufficient/transient response to fluids

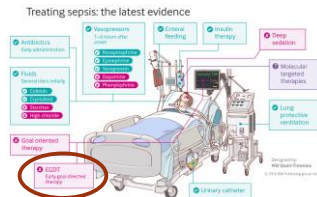


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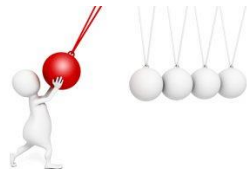


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EARLY GOAL DIRECTED THERAPY IN SEPSIS THE PENDULUM SWINGS...



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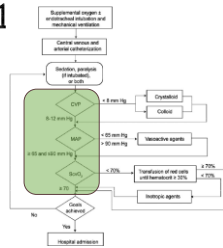
26

EARLY GOAL DIRECTED THX RIVERS 2001

263 patients

Mortality
30.5 % EGD^T
46.5 % Control

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PAPER

Low central venous oxygen saturation is associated with increased mortality in critically ill dogs

G. M. Hayes*, R. Mathews, S. Brontcrast and C. Diversi

Journal of Veterinary Emergency and Critical Care

Original Study

Changes in tissue perfusion parameters in dogs with severe sepsis/septic shock in response to goal-directed hemodynamic optimization at admission to ICU and the relation to outcome

Andreza Conti-Pantara, DVM, MSc, PhD; Juliana de Araújo Caldeira, DVM; Ewaldo de Mattos-Junior, DVM, MS; Haley da Silva de Carvalho, DVM, MSc; Adriane Reimoldes, DVM; Bruno Greguarini Poltron, DVM; Marcelo Pantara, MS; Mariana Semedo Francisco Tallo, DVM; Marcelo Faustino, DVM; Clair Motos de Oliveira, DVM, MSc, PhD and Silvia Renata Gaudio Cortopassi, DVM, MSc, PhD

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EARLY GOAL DIRECTED THERAPY PUBLICATIES BIJ HONDEN



JSAP 2011 Hayes, Mathews

ScvO₂

PCV

MAP

T^{co}

SpO₂

~ Mortality

JVECC 2012 Conti-Pantara

ScvO₂

Lactate

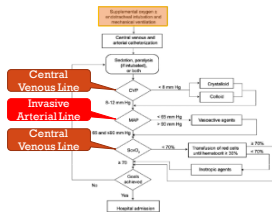
BP

~ Mortality

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An alternate pathophysiologic paradigm of sepsis and septic shock

Implications for optimizing antimicrobial therapy

Arunal Kumar

Section of Critical Care Medicine, Division of Infectious Diseases, Seattle Children's Hospital, University of Washington, Seattle, WA, USA

The advent of modern antimicrobial therapy following the discovery of penicillin during the 1940s yielded remarkable improvements in case fatality rate of serious infections including septic shock. Since then, pathogens have continuously evolved under selective antimicrobial pressure resulting in a lack of significant improvement in clinical effectiveness in the antimicrobial therapy of septic shock despite ever more broad-spectrum and potent drugs. In addition, although substantial effort and money has been expended on the development novel non-antimicrobial therapies of sepsis in the past 30 years, clinical progress in this regard has been limited. This review explores the possibility that the current pathophys-

ologic paradigm of septic shock fails to appropriately consider the primacy of the microbial burden of infection as the primary driver of septic organ dysfunction. An alternate paradigm is offered that suggests that has substantial implications for optimizing antimicrobial therapy in septic shock. This model of disease progression suggests the key to significant improvement in the outcome of septic shock may lie, in great part, with improvements in delivery of existing antimicrobials and other anti-infectious strategies. Recognition of the role of delays in administration of antimicrobial therapy in the poor outcomes of septic shock is central to this effort. However, therapeutic strategies that improve the degree of antimicrobial cidal-ity likely also have a crucial role.

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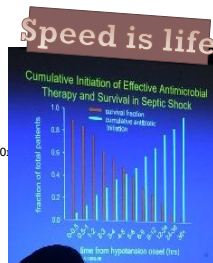
INFECTIOUS CONTROL

- Rivers EGD^T
 - Antibiotics given faster in the EGD^T group
- Kumar et al. Critical Care Medicine 2006
 - 5% of patients receive proper antibiotics within 30 min
 - 78% survival rate
 - Every 1 hour delay survival drops by 7,5%
- Confirmed in
 - Ferrer et al 2014
 - De Sousa 2008: 6(3); 323-327

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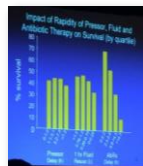
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INFECTIOUS CONTROL

- Wait until cultures performed
- Moving patients
- Lack of communication
- Lack of protocol
- Chain of command
- Forgotten
 - Didn't consider sepsis
 - Immunodeficiency...



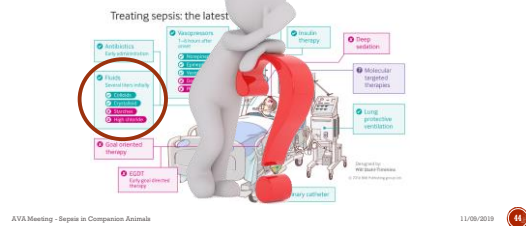
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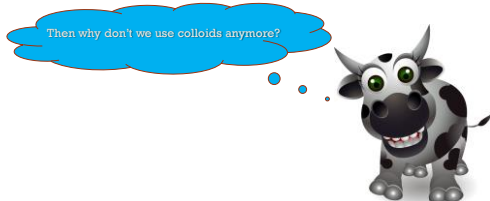
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SURVIVING SEPSIS CAMPAIGN 2016



SHOCK RESUSCITATION ISOTONIC – HYPERTONIC CRYSTALLOIDS



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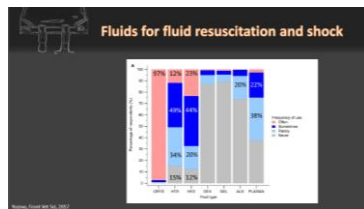
The fall of HES

- J. Boldt – one of the most *prolific advocates* of HES
- Examination of articles authored or co-authored by J. Boldt (since 1999...)
 - Missing ethical approval
 - No formal consent by study participants
 - False data reported
- Retraction** of 94 publications!
- No harm for the patients



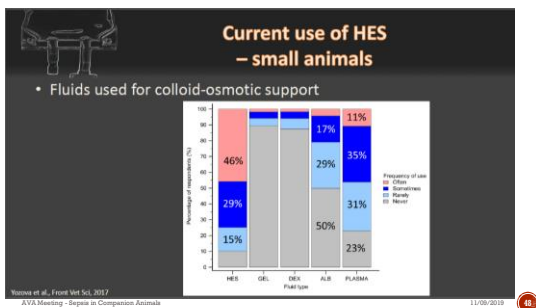
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THE COLLOID DEBATE



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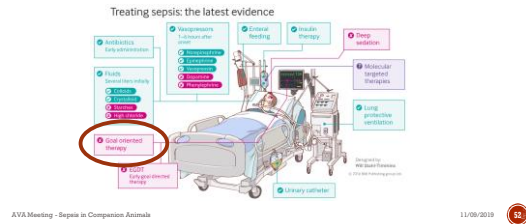
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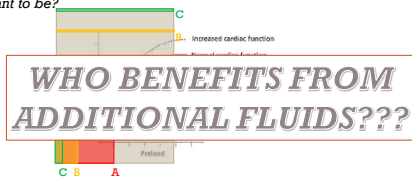
FRANK-STARLING

Who do you want to be?

Patient A

Patient B

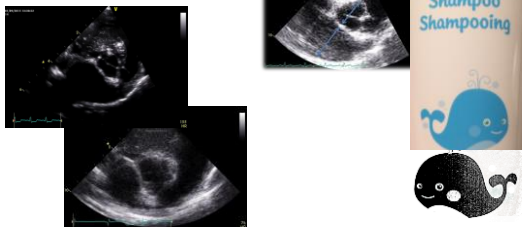
Patient C



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CHECK LA/AO

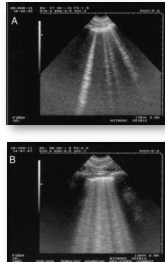


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CHECK LUNGS >3 B-LINES

- Comet-tail
- Starts at pleural line
- Moves with lungs
- Reaches to farfield
- Clear contours
- Crosses A-lines
- Hyperechogenic as pleural line



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PERSONALIZED CARE

- Fluid Assessment
- +
- Fluid Responsiveness
- +
- POCUS CVC
- +
- POCUS Lungs
- +
- POCUS Cardiac
- +
- Monitoring

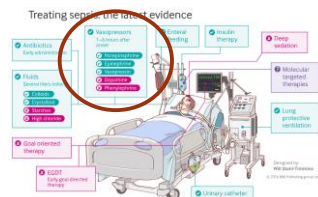


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SURVIVING SEPSIS CAMPAIGN 2016



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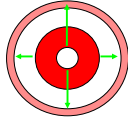
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PATHOGENESIS OF SEPTIC SHOCK

- Peripheral vasodilation
 - (decreased vascular systemic resistance)



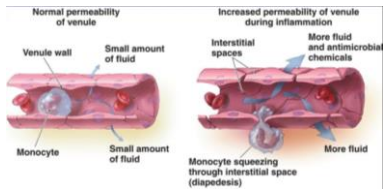
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PATHOGENESIS OF SEPTIC SHOCK



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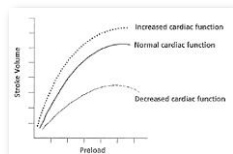


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VASOPRESSORS

- Vasopressors indicated sooner rather than later
 - Increase SVR
 - Also vasoconstriction
 - => **Increasing preload**
 - Frank-Starling
 - At the plateau SV may decrease
 - In the inclining part SV will increase



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PATHOGENESIS OF SEPTIC SHOCK CARDIAC FUNCTION

Despite correct resuscitation

- *Systolic function* ↓
- *Diastolic function* ↓
- *Ventricular dilation*

Impacts

- Prognosis
- Stabilization
 - *How do you approach a broken pump...?*



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MYOCARDIAL DYSFUNCTION/HIBERNATION

Ilary to

- *Inflammatory cytokines*
 - TNF- α
 - IL-1
- NO
- Calcium homeostasis
- ...

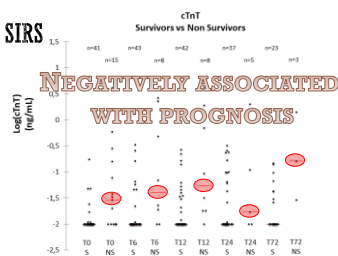


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CTNT IN SIRS



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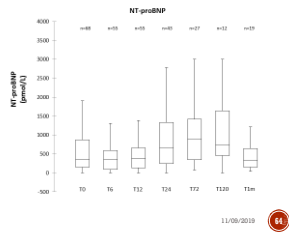
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NT-PROBNP IN SIRS

- Rises 24h to 120h after presentation
- NO clear link with prognosis

	T0	T6	T12	T24	T72	T120	T126
SB	1.7						
TS	0.012						
T12	0.026	0.049					
T24	0.006	0.006	0.001				
T72	0.006	0.006	0.001	0.006			
T120	0.005	0.005	0.001	0.006	0.006		
T126	0.005	0.005	0.001	0.006	0.006	0.006	0.006

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Public Emerg. Care. 2012 Oct;28(10):1982-5. doi: 10.1097/PEC.0b013e3182668666

Beneficial effects of levosimendan in infants with sepsis-associated cardiac dysfunction: report of 2 cases.

Pisoffi P, Caracciolo E, Versacci F, Piro B, Morici G, Moliterni A

@ Author information

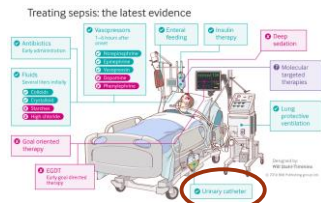
Abstract

Although international guidelines for hemodynamic support of pediatric septic shock suggest considering the potent calcium sensitizer inodilator levosimendan as a second-line inotropic agent to treat cold hypodynamic shock resistant to catecholamines, clinical experience in septic infants is lacking. We report the beneficial effects of levosimendan infusion in 2 infants (39 and 64 days old) with low cardiac output septic shock (ejection fraction, 25% and 33%; fractional shortening, 10% and 16% respectively) refractory to volume replacement and to the catecholamines dopamine and dobutamine. Levosimendan infusion (0.15 µg/kg/min) promptly increased both patients' myocardial contractility and improved tissue perfusion, thereby reducing lactate levels and increasing urine output. The only adverse effect was moderate hypotension in one infant, who reversed by adding norepinephrine to levosimendan. This clinical experience confirms the potential beneficial effects of levosimendan infusion to restore hemodynamics in infants with low cardiac output septic shock resistant to catecholamines.

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URINARY OUTPUT

- Information about
 - Fluid status
 - Renal function
 - Early alarm signal!!!
 - Azotemia
 - Electrolytes
 - Volume overload
 - Dehydration
- Risk
 - Infection!!!



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WAS THIS RELEVANT?

Implementation of the Surviving Sepsis Campaign guidelines

Vikramjit Mukherjee and Laura Evans

Purpose of review
Early identification and appropriate management of sepsis improves outcomes. Despite convincing data showing the benefits of early recognition and treatment of sepsis and septic shock, implementation of such evidence-based therapy is suboptimal. This review describes methods that have been shown to improve bedside application of the evidence-based guidelines.

Recent findings
The Surviving Sepsis Campaign (SSC) has developed guidelines for the management of severe sepsis and septic shock. The initial SSC guidelines were published in 2004, as evidence continued to evolve, the guidelines were updated, with the most recent iteration published in 2016. Guidelines by themselves can take years to change clinical practice. To affect more rapid change, the SSC guidelines are filtered into bundles to impact behavior change in a simple and uniform way.

Summary
Implementation of the SSC bundles revolves around practice improvement measures. Hospitals that have successfully implemented these bundles have consistently shown improved outcomes and reductions in healthcare spending. Finally, the Centers for Medicare and Medicaid Services has approved SSC bundle compliance as a core measure, and hospitals in the United States are mandated to collect and report their data regularly to Centers for Medicare and Medicaid Services.

Keywords
bundles, education, regulatory efforts, sepsis

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10.45 – 11.30

Fluid therapy in small animals

(K. Gommeren)



Be aware that this presentation
may have been adapted until
the very last minute prior to
the presentation 😊
All apologies for the
inconvenience

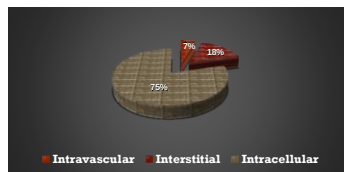
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TOTAL BODY WATER

- 60% of BW
- (80% in neonates)

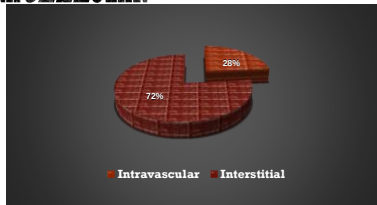


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BODY WATER EXTRA^{CELLULAR}

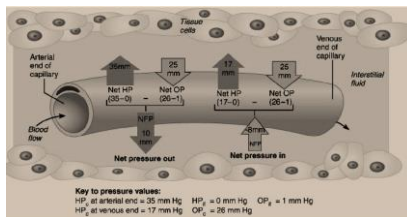


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STARLING'S LAW

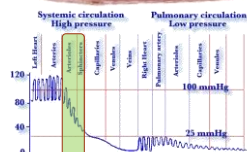
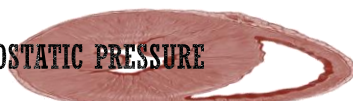


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HYDROSTATIC PRESSURE



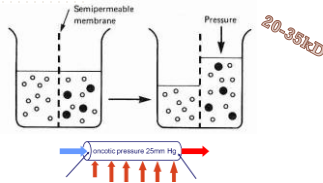
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ONCOTIC PRESSURE COLLOID OSMOTIC PRESSURE

Albumine / globuline / fibrinogen

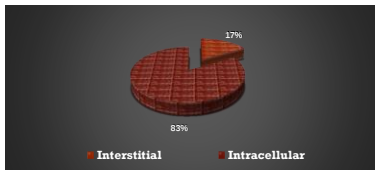


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BODY FLUID EXTRA VASCULAR

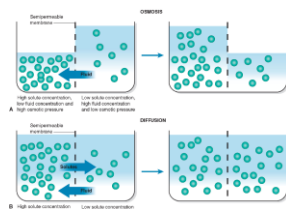


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OSMOTIC PRESSURE

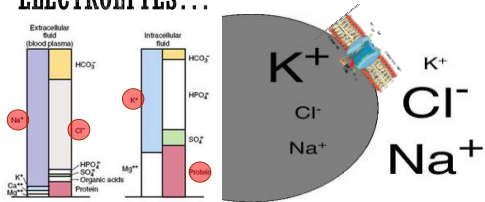


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EXTRA VS INTRACELLULAR ELECTROLYTES...

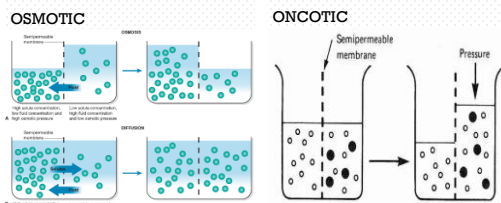


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OSMOTIC VS ONCOTIC PRESSURE



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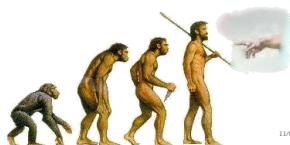


OPTIONS

- Hypotonic fluids
- Isotonic crystalloids
 - Replacement fluids
 - Maintenance fluids
- Hypertonic crystalloids
- Colloids
 - HES
 - Dextranes
- Blood products
 - Plasma
 - pRBCs (Human albumin)
- Oxyglobin

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ISOTONIC CRYSTALLOIDS

HARTMAN/NACL/RINGERS/PLASMAYTE

- Isotonic $\approx$ 300 mOsm/L
 - $[Na^+] > 140$ mEq/L
 - $H_2O +$
 - Electrolytes +/-
 - Buffer
- Perfect exchange IV - IS
 - Electrolytes 23D
 - Glucose 180D
 - Within 30 min

Product	Osmol. mOsm/L	Na ⁺ mEq/L	Cl ⁻ mEq/L	K ⁺ mEq/L
Hartman	299	140	98	5
NaCl 0.9%	310	155	155	0
Ringers	273	130	109	4

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ISOTONIC CRYSTALLOIDS

HARTMAN/NACL/RINGERS/PLASMAYTE

- NaCl 0.9%
 - $[Na^+] >$ plasma
 - $[Cl^-] >>>$ plasma
 - For daily use requires compensation
 - Might be nice in case of cerebral contusion
- Severe acidosis calls for a buffer
 - Lactate to be avoided when liver failure
 - Acetate
 - ...



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ISOTONIC CRYSTALLOIDS

HARTMAN/NACL/RINGERS/PLASMAYTE

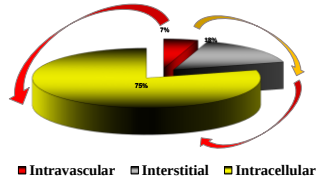
- $\uparrow\uparrow\uparrow$ IS compartment
 - Interstitial-  Edema
 - Intracranial-
 - Pulmonary-
- Hemodilution
 - Hypoproteinemia  Colloids
 - Anemia  pRBC's
 - Hypocoagulability  Plasma

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ISOTONIC CRYSTALLOIDS HARTMAN/NaCl/RINGERS/PLASMA-LYTE



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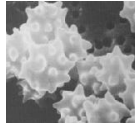


HYPERTONIC SALINE

- $[Na] \gg \text{plasma}$
- H_2O interstitial/intracellular shifts intravascularly
 - Restored balance within 30 min
 - Often requires follow-up administration

- Dose
 - NaCl 7,5% 4-6 mL/kg
 - NaCl 8% 8-12 mL/kg

Never when dehydrated



HYPOVOLEMIA

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HYPERTONIC SALINE

- Indications
 - Hypovolemia (trauma...)
 - Headtrauma
 - Pulmonary contusions

Additional benefits

- CV-system
 - Increased preload
 - + inotrope
 - Improves microcirculation
- Immune system
 - Decreased neutrophil burst activity
 - Modulation cytokines
 - Oxygen radical scavenger

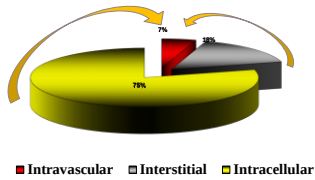


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HYPERTONIC SALINE

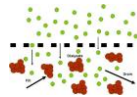


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COLLOIDS



- Molecules > 35 kD
 - Proteins
 - Plasma
 - Human albumin
 - Oxyglobin
 - Carbohydrates
- Interstitium = 1 mmHg
- Intravascular = 25 mmHg

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COLLOIDS

VOLOVEN - HAES



- Starches
 - Larger molecular weight
 - Higher MW equals prolonged halflife
 - Fewer particles = decreased "pull"
 - DOS : Degree of substitution
 - Amount of starches with hydroxylations on C2 or C6
 - Higher DOS equals prolonged halflife
- Indications
 - Hypovolemia/hypotension
 - Hypoproteinenia
 - Leakage/vasculitis
 - Sepsis
 - Anaphylaxis



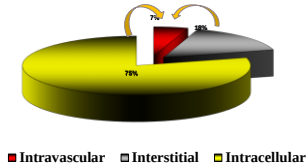
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COLLOIDS

VOLUME - HAES



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COLLOIDS

VOLUME - HAES

- Risks
 - Coagulopathy
 - Platelet/VwF/Factor XIII function
 - Prolonged APTT and platelet closure time
 - Product & dose dependent



- 20 mL/kg/d

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COLLOIDS

VOLUME - HAES

- Risks
 - CV Overload
 - ↑ Viscosity
 - ↑ Peripheral resistance
 - ↑ Afterload

- 20 mL/kg/d



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COLLOIDS

VOLUVEN - HAES

Risks

(ARF)

- Larger molecules
- Fluid shifts
 - Decreasing GFR
 - Hypertonic glomerular filtrate
 - Dehydrates proximal tubular cells
 - Direct toxicity after deposit in renal cells

[Anaphylactic shock (0.033%)]

- (gelatines < carbohydrates < dextrans)



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FLUID THERAPY IN PRACTICE

Dehydration



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Hypovolemia



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FLUID LOSS DEHYDRATION

Clinical Exam

- Mucous membranes
- Eye position
- Skin fold

Complementary Exam

- Hct/PCV
- T-pro/album
- Azotemia
- Urine specific gravity



PERCENT DEHYDRATION	PHYSICAL SIGNS
<2%	Not detectable
3-6%	Mild loss of skin elasticity
6-8%	The above + dry muc., depressed glides within orbit
8-10%	The above + more persistent skin tent, increased PCV/TP
10-12%	The above + dry pale muc., CRT >2sec
>12-15%	Signs of shock, death

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DEHYDRATION

- Substitute slowly
- Faster evolution = More aggressive therapy
 - Isotonic crystalloids
 - Calculation

• ~%	Dehydration	(Estimation)
• X	Weight	(Exact)
• /	Desired time	(Choice)
• +	Maintenance	(Relative)
• +	Ongoing losses	(Estimation)

Fat/Large/Old/Cardiac
Soften rates

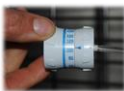
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FOLLOW-UP DAILY FLUID PLAN

- Clinical parameters
 - Skin fold
 - Eye position
 - Moisture mucous membranes
- Complementary exam
 - T-pro
 - Albumine
 - Ureum/Creatinine
 - Urine specific gravity
 - Urine production
 - Weight evolution



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INTRAVASCULAR
FLUID DEFICIT

- Vasoconstriction
- Pale
- Tachycardia
- Weak Pulse
- CRT ↑
- Cold extremities



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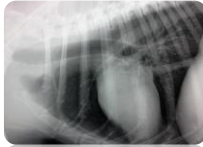


RESUSCITATION? EVALUATE SHOCK

- Decreased systolic blood pressure

SAP $<90\text{mmHg}$
 $<80\text{mmHg}$

Lactate $>2,0\text{mmol/L}$
 $>2,5\text{mmol/L}$



BACK TO
BASICS

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FLUID RESUSCITATION TYPES OF SHOCK

- Hypovolemic
- Obstructive
- Distributive
- Cardiogenic



RESUSCITATION

=> NO RESUSCITATION!!!



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EFFECTS OF RESUSCITATION FLUIDS

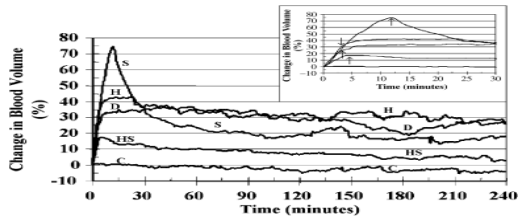
Fluid	Post-infusion ($P<0.05$)	30 minutes ($P<0.05$)	240 minutes ($P<0.05$)
0.9% saline (S)	76.4 $\pm$ 10.0% (HS, D, HES)	35.2 $\pm$ 9.3% (HS, C)	18.0 $\pm$ 9.7% (C)
7.5% saline (HS)	17.1 $\pm$ 3.2%	12.3 $\pm$ 0.9% (D, HES)	2.9 $\pm$ 6.1% (D, HES)
Dextran 70 (D)	23.0 $\pm$ 10.5%	35.9 $\pm$ 7.3% (C)	25.6 $\pm$ 16.1% (C)
Hetastarch (HES)	27.2 $\pm$ 6.4%	36.8 $\pm$ 6.5% (C)	26.6 $\pm$ 8.6% (C)
Control (C)	NA	-0.2 $\pm$ 8.8%	-3.7 $\pm$ 3.4%

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EFFECTS OF RESUSCITATION FLUIDS



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EFFECTS OF RESUSCITATION FLUIDS

Type	Dose	End	30min	4h
Isotonic	80mL/kg	(76%)	35%	19%
Colloid	20mL/kg	25%	36%	26%
Hypertonic	4mL/kg	17%	12%	3%

- Start with isotonic crystalloids
- Add or switch to whenever indicated/required
 - Low oncotic pressure → Colloid
 - Pulmonary-/Cerebral contusions → Hypertonic

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MONITORING SHOCK - INFUSION

- Clinical parameters
 - Heart rate
 - Pulse quality
 - Mucous membranes
 - Capillary refill time
 - Temperature gradient (rectal versus limb)
 - Mentation
 - (V. jugularis/saphena)
- Complementary exam
 - Blood pressure
 - Lactate
 - Central venous pressure



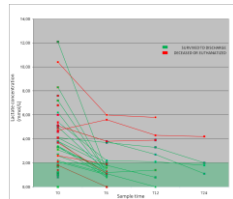
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LACTATE KINETICS

- Lactate $\uparrow$ whenever anaerobic metabolism
 - Important for emergencies
- Human medicine
 - Lactate ~ prognosis
 - Evolution most important
- Veterinary
 - Lactate ~ prognosis in ICU and GDV
 - (Lagutchuk, Ogilvie et al. 1998; de Papp, Drobatz et al. 1999)
 - Evolution most important
 - (Hei, Lobetti et al. 2004; Stevenson, Kidney et al. 2007)



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EGDT HEMODYNAMICS

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CRITICAL CARE Open Access

RESEARCH

A positive fluid balance is an independent prognostic factor in patients with sepsis

Angela Schenck and Ron-Look Vincent

Abstract

Introduction: Intravenous fluid administration is an integral part of sepsis management. However, fluid administration has been associated with both positive and negative outcomes. The purpose of this study was to determine if a positive fluid balance is an independent prognostic factor for mortality in sepsis patients.

Methods: We retrospectively analyzed 100 patients who were treated in our Department of Intensive Care.

Results: Of the 100 patients, 50 died (50%). Mean daily fluid balance was 1.5 L (range -0.5 to 4.0 L). Patients with a positive fluid balance had a significantly higher mortality rate (p = 0.001) compared to patients with a negative fluid balance.

Conclusion: Persistence of a positive daily fluid balance over 72 hours was strongly associated with increased mortality in sepsis patients.

Fluid Overload in Patients with Severe Sepsis and Septic Shock Treated with Early-Goal Directed Therapy is Associated with Increased Acute Need for Fluid-Related Medical Interventions and Hospital Death

Diana J. Kalin, MD^{1,2}, Jared T. Perrin, MD¹, Rodrigo Carlin-Celis, MD^{1,2}, Ognjen Gajic, MD^{1,2}, Louis Schenck, MS³, and Cassie C. Kennedy, MD^{1,2}

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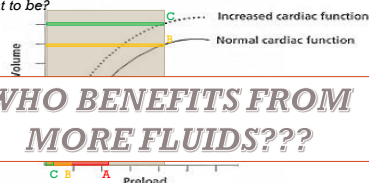
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FRANK-STARLING

Who do you want to be?

Patient A
Patient B
Patient C



WHO BENEFITS FROM MORE FLUIDS???

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HOW DO YOU PERFORM FLUID RESUSCITATION? ISOTONIC CRYSTALLOIDS

- ↑↑↑ Extravascular compartment
 - Pulmonary
 - Interstitial edema
 - Intracranial
- Hemodilution
 - Anemia
 - Hypoproteinemia
 - Hypocoagulability

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FLUID OVERLOAD

- Fluid overload in critically ill human patients is associated with longer hospitalization, increased mechanical ventilation, acute kidney injury, abdominal compartment syndrome, organ dysfunction and increased mortality

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FLUID STEWARDSHIP

- There is a trend in the human profession towards what has been termed "fluid stewardship"
- The 4 D's of fluid therapy: drug, duration, dosing and de-escalation
- 4-phase "ROSE" fluid resuscitation strategy: resuscitation, optimization, stabilization and evacuation



FLUID STEWARDSHIP 3 POINTS TO FEAR

- The heart (lungs)
- Oncotic pressure (dose)
- Vessel integrity (efficiency)



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FLUID STEWARDSHIP THE HEART

- Cardiac Congestion
 - Preload/Afterload ↑
 - Venous hydrostatic pressure ↑
 - Pulmonary edema
 - Pleural effusion
 - Ascites

→ Inadvertent administration of shock boluses is dangerous!!



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FLUID STEWARDSHIP ONCOTIC PRESSURE

- Large quantities of crystalloids
 - Oncotic pressure ↓
 - Peripheral edema
 - Pleural effusion
 - Ascites

→ Shock doses become less efficient after **20 minutes**

(However, your patient may suffer from ongoing fluid loss???)

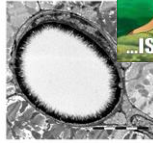
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FLUID STEWARDSHIP THE VESSELS

- Endothelium 'normally' permeable for
 - H_2O
 - Electrolytes
 - Urea
 - Small proteins/hormones/...
- Leakage
 - Extravasation
 - Albumine
 - RBCs
- → Hemorrhage (80 mmHg < PAM > 100mmHg)



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ISOTONIC CRYSTALLOIDS SWITCHING TO BOLUS ADMINISTRATION

• DOG	80-90mL/kg/h bolus 10-20mL/kg over 5-10min
• CAT	40-50mL/kg/h bolus 10-15mL/kg over 10-15min

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DEFINING A FLUID BOLUS

- Ideal fluid bolus would be ...
 - a discrete volume *
 - of a specific fluid *
 - administered at a specified rate*
 - accounting for individual patient features
 - and with a defined aim (i.e. increase the stroke volume by at least 10-15% and improve organ perfusion)



- There is no current agreement regarding exactly what defines a fluid bolus

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Defining the characteristics and expectations of fluid bolus therapy:
A worldwide perspective^{1,2,3,4,5,6,7,8,9,10}

- Intensive care specialists in 30 countries
- 3138 responses

Volume of fluid							
Fluid type	<100 mL	>125 mL	>250 mL	>500 mL	>750 mL	>1000 mL	
Crystalloids							
0.9% saline	56 (31)	41 (20)	673 (368)	713 (395)	32 (28)	313 (185)	
n (%)	56 (31)	41 (20)	673 (368)	713 (395)	32 (28)	313 (185)	
Range	0-215	0-100	0-400	70-715	0-35	0-400	
Defining the fluids acceptable for use as fluid bolus therapy							
Region	41% albumin	20% albumin	88%	Crystalloids	0.9% saline	CS	Acetate
Overall proportion	1182 (40)	623 (21)	489 (17)	269 (9)	1908 (73)	1673 (72)	1729 (65)
Highest national proportion	55%	62%	62%	88%	100%	98%	98%
Lowest national proportion	10%	13%	6%	8%	20%	34%	44%
Median (IQR)	43% (30%-61%)	30% (27%-45%)	21% (11%-35%)	32% (7%-44%)	70% (60%-90%)	72% (60%-82%)	68% (50%-81%)
Rate of acceptance							
Fluid type	<100 mL	100-250 mL	250-500 mL	>500 mL	>750 mL	>1000 mL	
Crystalloids							
0.9% saline	844 (28)	815 (48)	114 (6)	54 (3)	12 (1)	7 (0)	
n (%)	844 (28)	815 (48)	114 (6)	54 (3)	12 (1)	7 (0)	
Range	100-700	0-400	0-200	0-170	0-45	0-25	

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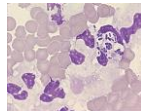
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PREDICTING IV VOLUME & FLUID RESPONSE

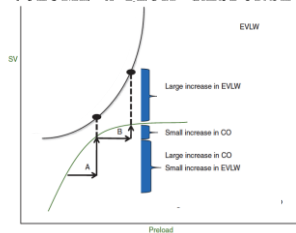
- Fluid responders vs non-responders
- Fluid losses and hypovolemia: excellent fluid responders
- Arterio- and venodilation together with microcirculatory and myocardial dysfunction: poor fluid responders (50% of patients)



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PREDICTING IV VOLUME & FLUID RESPONSE



British Journal of Anaesthesia, 116 (3): 339-49 (2016)

me?
ion, etc) improve following



11

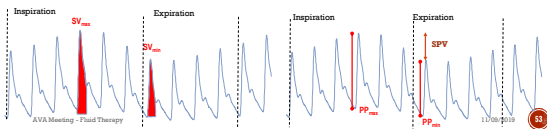
PREDICTING IV VOLUME & FLUID RESPONSE

- Cardiac Output and/or stroke volume
- Gold standard
 - Multiple techniques
 - Both invasive (thermo-dilution) and non-invasive (trans esophageal echo etc.)
 - Limited availability and can be time consuming



PREDICTING IV VOLUME & FLUID RESPONSE

- Dynamic indexes
 - Positive pressure ventilation and respiratory variations in
 - stroke volume
 - systolic pressure
 - pulse pressure
- Patients with a PPV > 13% may be relatively hypovolemic and respond to a fluid bolus (the greater the variation the more likely the patient is a responder)



DYNAMIC INDEXES IN DOGS

2017

Accepted Manuscript

Evaluation of the dynamic predictors of fluid responsiveness in dogs receiving goal-directed fluid therapy

Maja J. Drozdyszynska, Yu-Mei Chang, Giacomo Stancani, Ludovico Pellgard



- Early goal directed therapy (10 ml/kg isotonic fluid over 10 minutes)
- A PPV > 13% or above reliably predicted cardiovascular response to fluid loading in 82.8% of canine cases undergoing abdominal surgery

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44

J Vet Emerg Crit Care (San Antonio). 2018 Jul;28(4):301-309. doi: 10.1111/vec.12728. Epub 2018 Jun 13.

Evaluation of pulse pressure variation and pleth variability index to predict fluid responsiveness in mechanically ventilated isoflurane-anesthetized dogs.

Sano T¹, Sato J¹, Wightman P¹, Cave NJ¹, Gosling MB², Johnson CB³, Chambers P¹.

Vet Anaesth Analg. 2017 Nov;44(6):1303-1312. doi: 10.1016/j.vaa.2017.07.007. Epub 2017 Aug 25.

Plethysmography variability index for prediction of fluid responsiveness during graded haemorrhage and transfusion in sevoflurane-anesthetized mechanically ventilated dogs.

Endo Y¹, Kawase K¹, Miyasho T², Sano T³, Yamashita K¹, Muir WW⁴.

J Vet Med Sci. 2017 Aug;78(8):1437-1443. doi: 10.1292/jvms.16-0287. Epub 26/7 Jul 10.

Stroke volume variation (SVV) and pulse pressure variation (PPV) as indicators of fluid responsiveness in sevoflurane anesthetized mechanically ventilated euolemic dogs.

Endo Y¹, Tamura J¹, Ishizuka T², Itami T², Hanazono K², Miyoshi K¹, Sano T³, Yamashita K¹, Muir WW⁴.

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LIMITATIONS OF DYNAMIC VARIABLES

- Mechanically ventilated
- Arterial line in most cases
- Ideal tidal volume?
- Ideal PIP?
- Ideal PEEP?



- Spontaneous respirations
- Arrhythmias
- Right heart failure
- Chest wall compliance
- Intra-abdominal pressure
- Pressure curve artifact

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Fischer et al. *Ann Intensive Care* (2016) 6:49
DOI 10.1186/s13613-016-0168-2

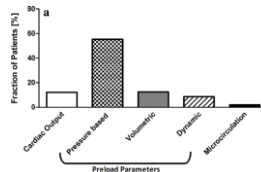
Annals of Intensive Care

RESEARCH

Open Access

Practice of hemodynamic monitoring and management in German, Austrian, and Swiss intensive care units: the multicenter cross-sectional ICU-CardioMan Study

- 1789 patients
- Invasive arterial 77.9 %
- Central venous catheterization 55.2 %
- Cardiac output 12.3 %
- Echocardiographic examination 1.9 %



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ROLE OF ULTRASOUND TO PREDICT
BLOOD VOLUME & FLUID RESPONSE
IN VETERINARY MEDICINE?



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The Journal of TRAUMA® Injury, Infection, and Critical Care

Hypovolemic Shock Evaluated by Sonographic Measurement
of the Inferior Vena Cava During Resuscitation in
Trauma Patients

Yasuichi Yamagawa, MD, PhD, Toshikazu Sakamoto, MD, PhD, and Yoshiaki Okada, MD, PhD 2007

- Poor IVC dilation following fluid resuscitation, may indicate inadequate blood volume despite a normal blood pressure
- IVC diameter a better predictor of recurrence of shock than blood pressure, heart rate, or arterial base excess?



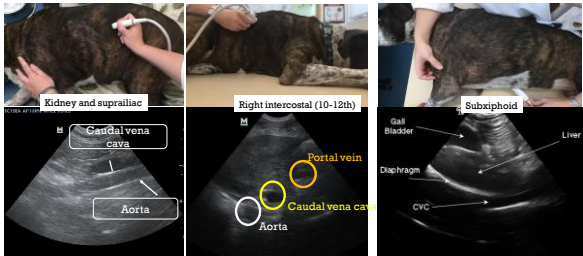
	Normovolem Group	Hypovolem Group	p
Systolic blood pressure (mm Hg)	105.9 ± 5.8	113.5 ± 3.8	NS
Heart rate	103.3 ± 4.8	107.5 ± 4.0	NS
Value of base excess (mEq/L)	-4.0 ± 1.0	-3.5 ± 0.9	NS
Value of hematocrit (g/dL)	9.0 ± 0.6	9.5 ± 0.6	NS
Diameter of inferior vena cava (mm)	8.5 ± 0.5	10.7 ± 0.7	<0.001
Diameter of IVC multiplied by BMI	143.6 ± 12.0	218.1 ± 10.4	0.0001

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VETERINARY MEDICINE: CAUDAL VENA CAVA



DYNAMIC INFERIOR VENA CAVA MEASUREMENT

- The thin wall and elastic nature of the CVC makes it a responsive and dynamic blood vessel
 - Size and geometry fluctuate in response to relative and absolute intravascular volume changes depending on the respiratory and cardiac cycle

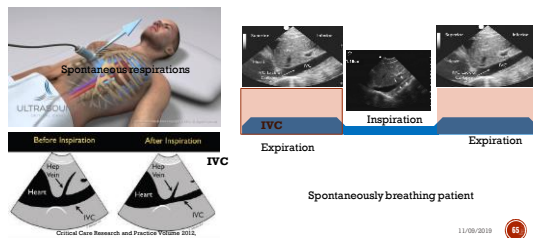


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DYNAMIC IVC COLLAPSIBILITY INDEX (IVC-CI)

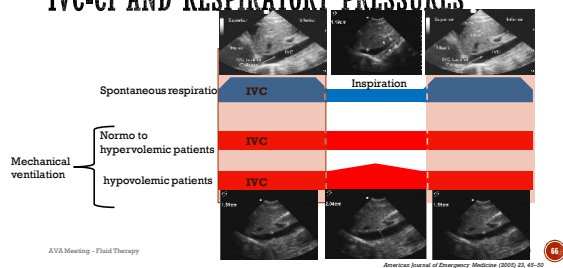


Critical Care Research and Practice Volume 2012

11/09/2019



IVC-CI AND RESPIRATORY PRESSURES



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American Journal of Emergency Medicine (2015) 25, 45–50



IVC-CI, VOLUME STATUS AND OUTCOME

- CVC diameter correlates with volume status and outcome in human patients

Int Surg. 2012 Dec;76(12):1386-6. Flat inferior vena cava: indicator of poor prognosis in trauma and acute care surgery patients. Chenard P¹, Weidert F¹, Auerbach J¹, Steyer J¹, Weber L¹, Weber M¹.
Am J Emerg Med. 2014 Dec;30(6):1414-1418.e1. doi: 10.1016/j.ajem.2011.10.017. Epub 2012 Jan 4. Role of inferior vena cava diameter in assessment of volume status: a meta-analysis. Geel A¹, Sauer Z¹, Surana A¹, Chandra S¹.
Int J Emerg Med. 2015 Mar;20(2):10-6. doi: 10.1007/s10240-014-014-0. Epub 2014 Dec 19. The role of inferior vena cava diameter in volume status monitoring: the best sonographic measurement method? Chenard P¹, Weidert F¹, Auerbach J¹, Steyer J¹, Weber L¹, Weber M¹, Chaurand P¹, Auerbach J¹, Steyer J¹, Weber L¹, Weber M¹.

- Changes
 - < 20% are associated with hypervolemia
 - > 60% are associated with hypovolemia

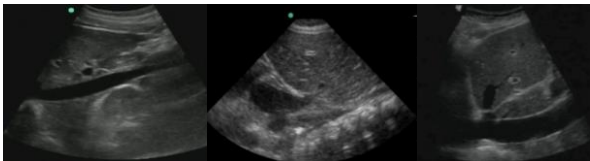
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NORMO, HYPO AND HYPERVOLEMIC: HUMANS

Spontaneously breathing patients
Trauma Association of Canada, Fairmont Vancouver, 2017, spontaneously breathing patients



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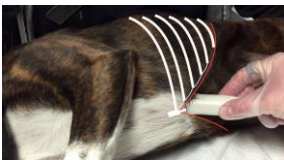
11/09/2019



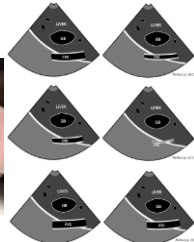
DYNAMIC CVC CHANGES IN VET. MED.

When measured in proximity to the heart/thorax

- Subxiphoid view



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30/2019



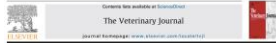
RIGHT INTERCOSTAL VIEW

DOI: 10.1186/s12917-019-1743-4; doi: 10.24004/1772-107

Correlation of the ratio of caudal vena cava diameter and aorta diameter with systolic pressure variation in anesthetized dogs.

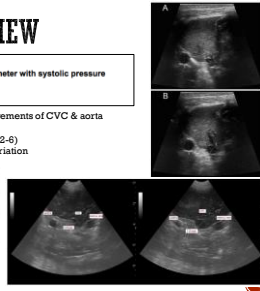
Marmoretti G, Rabreau R, Franco P.

Static measure as ventilation was suspended to get measurements of CVC & aorta
 A = prefluid hypovolemic healthy dog under anaesthesia
 B = same dog post 3-4 ml/kg fluid boluses over 1 minute (2-6)
 CVC:aortic ratio correlates with systolic pulse pressure variation



Original Article
 Respiratory variation in aortic blood peak velocity and caudal vena cava diameter can predict fluid responsiveness in anaesthetized and mechanically ventilated dogs

Marmoretti G, Rabreau R, Franco P, Rabreau R, Franco P
 24% for CVCDI (sensitivity, 77.78%; specificity, 73.33)
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Received: 13 December 2017 | Revised: 14 February 2018 | Accepted: 27 March 2018

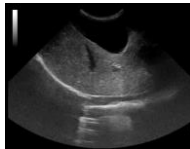
DOI: 10.1111/jvim.15036

STANDARD ARTICLE

Journal of Veterinary Internal Medicine **ACVIM**

Establishment of reference values of the caudal vena cava by fast-ultrasonography through different views in healthy dogs

Elodie Damiot¹ | Sören Boyen² | Anne-Christine Mervielles¹ |
 Loïc Desquilbet¹ | Serge Chalhoub¹ | Kéris Gommers¹



Poor inter-rater variability
 Easy to obtain
 CVC-I mean: 0.30 ± 0.12
 AVA Meeting - Fluid Therapy



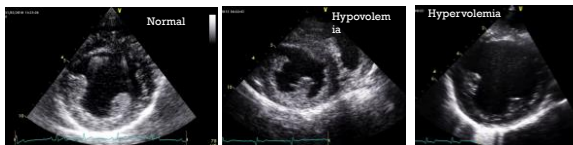
More difficult to obtain
 Good inter-rater variability

11/05/2019

CARDIAC VOLUME STATUS IN VET. MED.

- LV wall thickening, decreased LA size, and decreased LV cavity appear to be a useful for the evaluation of hypovolemia in dogs

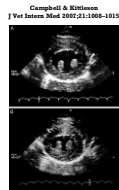
Echocardiographic Findings in Dogs with Hypovolemia
 International Veterinary Emergency and Critical Care Symposium 2005
 S.B. DePaola, J.E. Rush, C.A. Boscato, D.J. Brown, L.H. Freeman



CARDIAC VOLUME STATUS IN VET. MED.



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Goughall & Kintner
J Vet Intern Med 2007;21:1098-1015

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CONCLUSIONS

- Little consensus on fluid boluses in veterinary medicine
- Fluid boluses to be balanced against risk of volume overload
- Cardiac output and stroke volume are gold standards for determining fluid responders (10-15% increase)
- Dynamic variables are accurate but limited to ventilation
- Point of care ultrasound maybe useful in spontaneously breathing veterinary patients but requires further study



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POINT OF CARE ULTRASOUND: FLUID RESUSCITATION GUIDE

6 CVC, HEART AND LONG ULTRASOUND – ROLE IN VETERINARY MEDICINE?

CVC and heart normal



Fluid challenge
Consider crystalloid – may help and unlikely to harm
Consider dynamic fluid responsiveness test

FLUID RESPONSIVENESS

2019





19TH EVECC CONGRESS GO WITH THE FLOW



AVA Meeting - Fluid Therapy

- International speakers
 - Advanced
 - Refresher
 - Nurse
- Resident focus
- ECC specialist
- Jean Louis Vincent

streams

11/08/2019



19TH EVECC CONGRESS GO WITH THE FLOW



- Different topics
 - Blood
 - Air
 - Urine
- Wetlabs
- Tubes and things
- Point Of Care
- Ultrasound
- ...

flow

11/08/2019





11.30 – 12.15

Acute kidney injury in small animals

(S. Cortellini)

Acute kidney injury

Stefano Cortellini

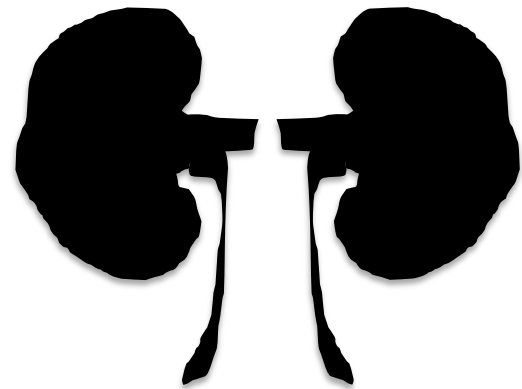
DMV, VetMed, Dipl. ACVECC, Dipl. ECVECC, FHEA, MRCVS
Recognised RCVS specialist in Emergency and Critical care
Lecturer in emergency and critical care
Royal Veterinary College
scortellini@rvc.ac.uk

Early recognition/
prevention

Early diagnosis

Tailored management

Follow-up



Early Recognition/ prevention

Acute renal failure

Acute kidney
injury



Is it only about the change of name?

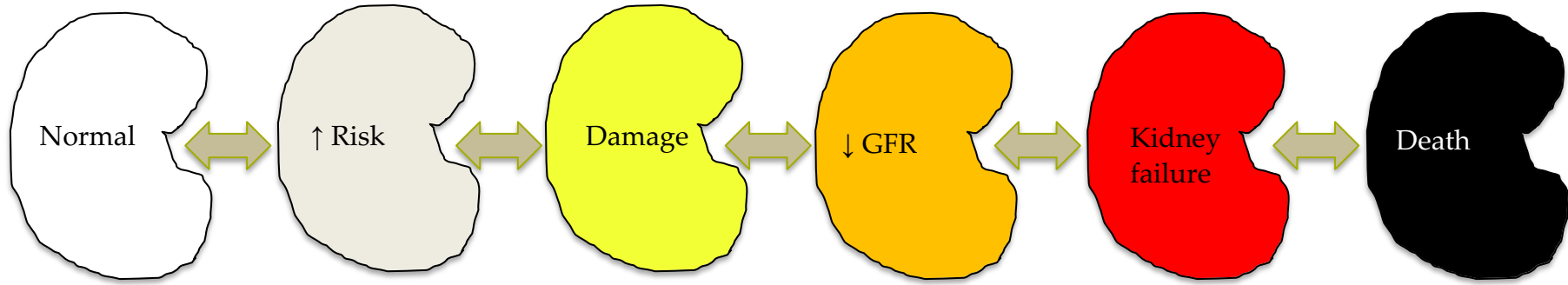
Renal disease: continuum of functional and structural abnormalities

- Wide spectrum
- Possible prevention
- Change of the therapeutic management
- Change of level of monitoring

15% of the hospitalised patients develop AKI¹
(1 every 6 patients):
54% of mortality (40-64%)



GFR



KDIGO guidelines

100%
50%

Initiation

- Tubular obstruction
- Ischaemia
- Hypoxia
- Inflammation
- Cellular injury

Extension

- Vascular damage
- Inflammation
- Coagulation dysfunction
- Ischaemia

Inflammation

Recovery

- Polyuria



AKI Grade	Blood creatinine	Clinical Description
Grade I	<1.6 (mg/dl) (<140 µmol/l)	Non Azotemic AKI: a. Documented AKI: (Historical, clinical, laboratory, or imaging evidence of acute kidney injury; clinical oliguria/anuria, volume responsiveness)... and/or b. Progressive non azotemic increase in blood creatinine; ≥ 0.3 mg/dl (≥ 26.4 µmol/l) within 48 hours c. Measured oliguria (<1 ml/kg/hr) or anuria over 6 hrs
Grade II	1.7 – 2.5 mg/dl (141 – 220 µmol/l)	Mild AKI: a. Documented AKI and static or progressive azotemia b. Progressive azotemic increase in blood creatinine; ≥ 0.3 mg/dl ≥ 26.4 µmol/l within 48 hours), or volume responsiveness* c. Measured oliguria (<1 ml/kg/hr) or anuria over 6 hrs
Grade III	2.6 – 5.0 mg/dl (221 – 439 µmol/l)	
Grade IV	5.1 – 10.0 mg/dl (440 – 880 µmol/l)	Moderate to Severe AKI: a. Documented AKI and increasing severities of azotemia and functional renal failure
Grade V	>10.0 mg/dl (>880 µmol/l)	

IRIS STAGING

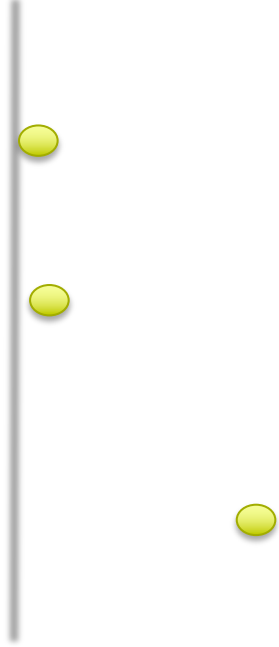
WWW.IRIS-KIDNEY.COM

VAKI stage	Criteria
Stage 0	Creat. increase <150%
Stage 1	Creat. increase 150-199% or increase of 26.5 µmol/l
Stage 2	Creat. increase 200-299%
Stage 3	Creat. increase >300% or an absolute creat. > 354 µmol/l (4 mg/dl)

Veterinary AKI

Thoen et al, 2011

Increase in creatinine by 26.5 µmol/l (0.3 mg/dl) in 48 h



Are there any other markers of AKI?

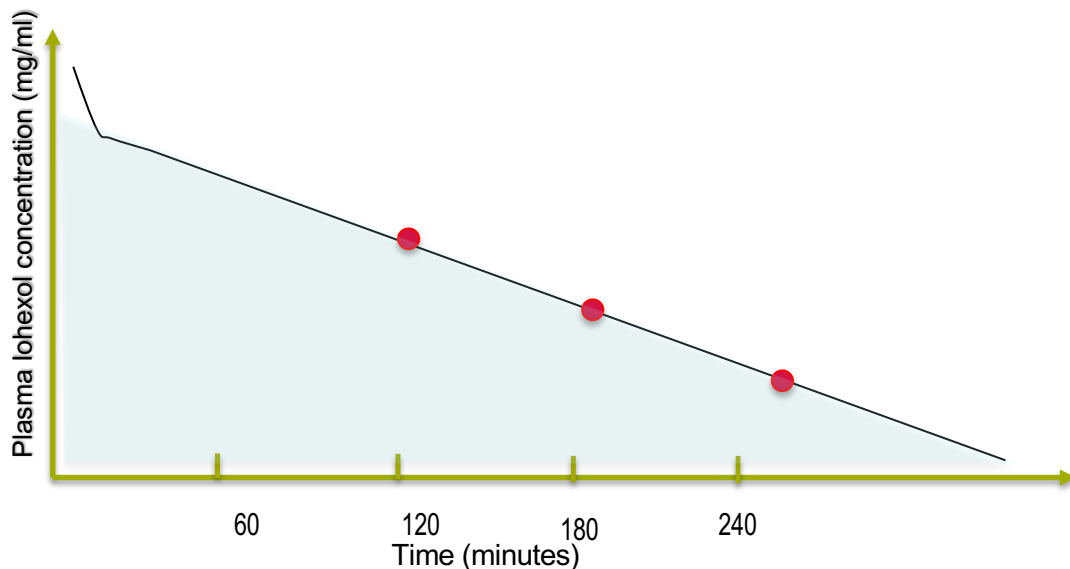
	<i>Cardiac disease</i>	<i>AKI</i>
1970s	Lactate dehydrogenase	Creatinine
1980s	Creatine-kinase MB	Creatinine
1990s	Troponin I, Troponin T	Creatinine
2000s	NT-proBNP	Creatinine

Creatinine = estimation of GFR

- Azotemia: 75% of nephron function lost
- Loss of urine concentration: > 66% nephron function lost
- Any other way of measuring/predicting GFR?

Plasma Iohexol clearance

- Clearance from the plasma a certain substance, which is renally excreted, is correlated with GFR



$$C_{\text{plasma}} = D / \text{AUC}$$

D= dose

AUC= Area under the curve

Useful in non azotemic patients

- Diagnosis of non azotemic CKD
- Progression of non azotemic CKD
- Adjustment of doses of drugs

Not real-time

Requires multiple blood samples

Other markers of GFR?

Cystatin C

- Low molecular weight (13 kDa)
- Non protein bound and renally excreted
- Controversial studies in people re superiority compared to creatinine to predict AKI
 - May be affected by pre-renal causes
 - No studies have assessed role of serum Cyst C in dogs with AKI
- No commercial assay available for benchtop measurement

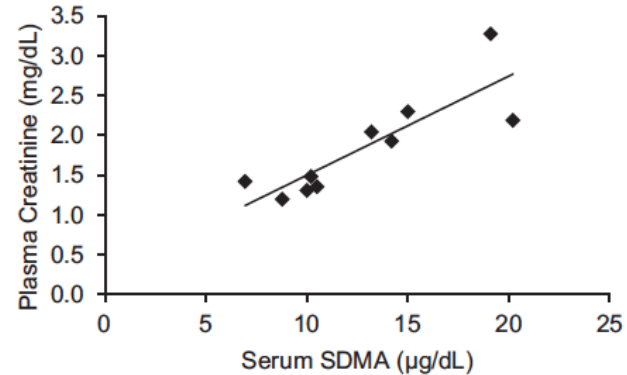
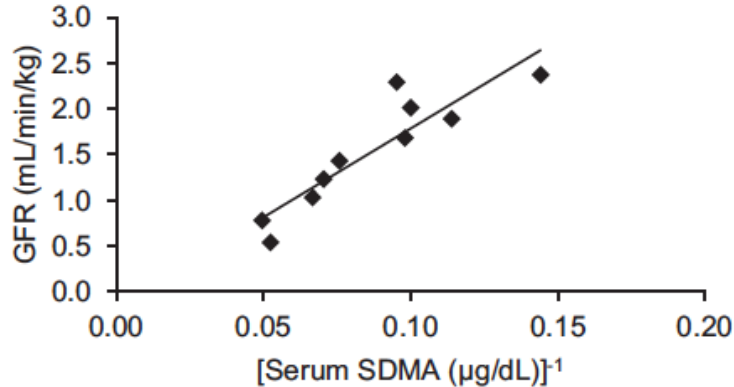
Other markers of GFR?

Symmetric Dimethylarginine (SDMA)

- Dimethylated derivative of arginine released in the circulation
- Renally excreted
- Well correlated with plasma creatinine

Relationship between Serum Symmetric Dimethylarginine Concentration and Glomerular Filtration Rate in Cats

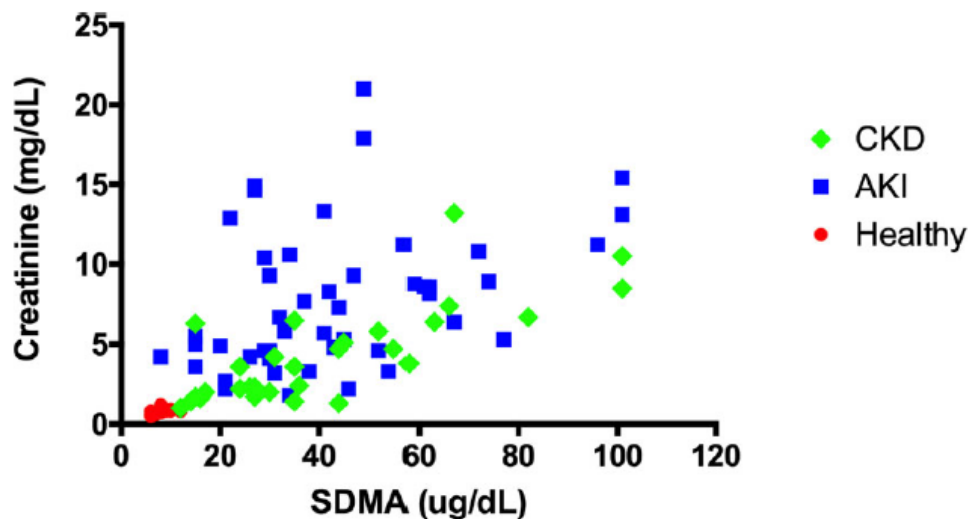
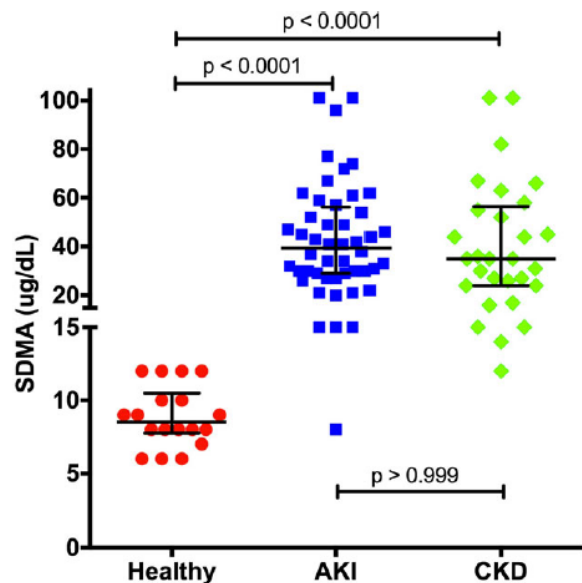
J. Braff, E. Obare, M. Yerramilli, J. Elliott, and M. Yerramilli

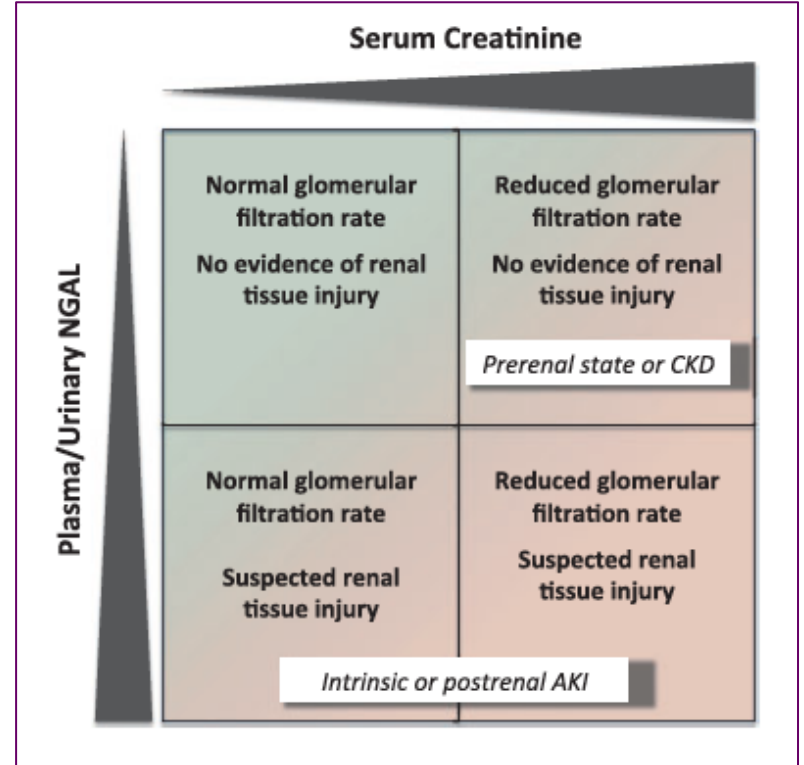


- 10 cats with CKD patient (azotemic and non azotemic)
- In non azotemic/azotemic cats linear relationship of reciprocal of SDMA ($1/\text{SDMA}$) and GFR (similarly to creatinine)

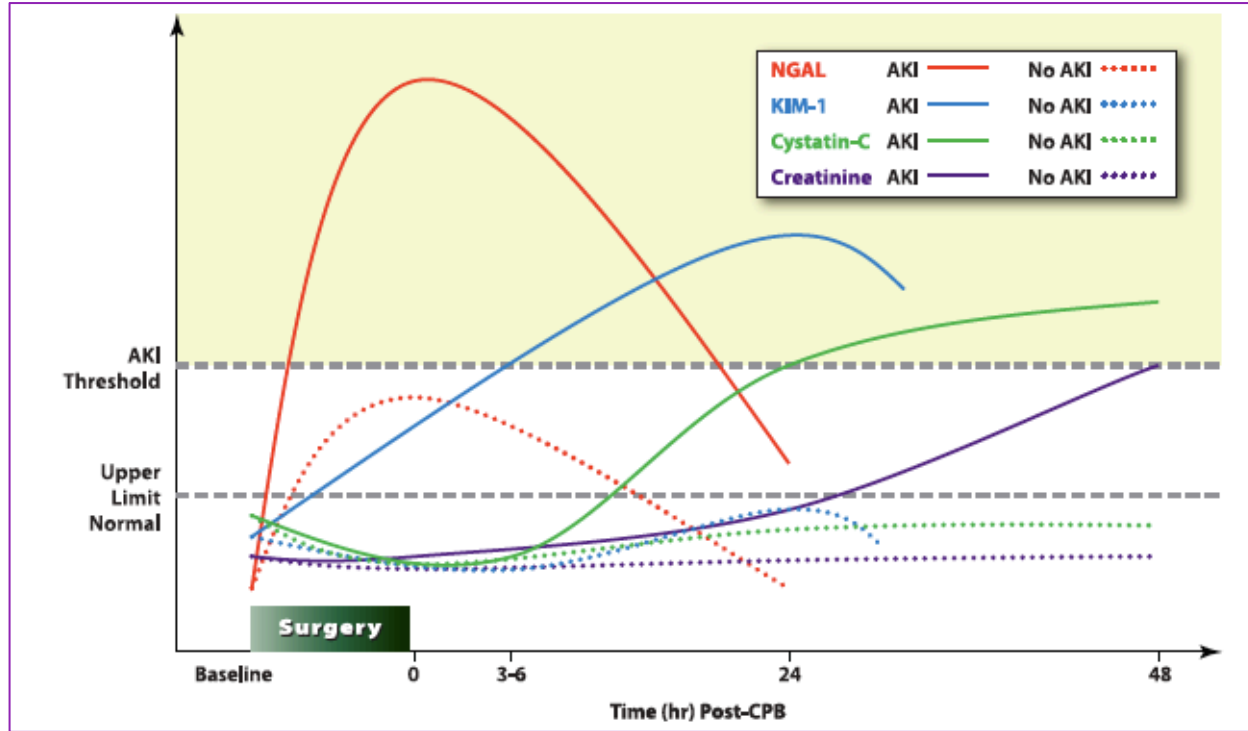
Plasma Symmetric Dimethylarginine Concentration in Dogs with Acute Kidney Injury and Chronic Kidney Disease

D.P. Dahlem , R. Neiger, A. Schweighauser, T. Francey, M. Yerramilli, E. Obare, and S.M.L. Steinbach 

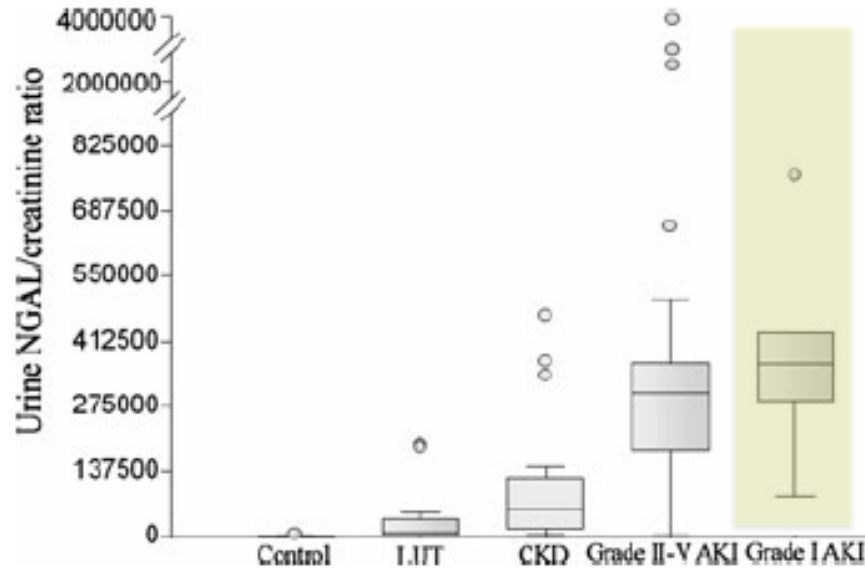




Function vs Injury



NGAL, KIM-1, NAG...



Segev G. et al, *JVIM*, 2013; 27:1362-67

Acute kidney injury

Hospital acquired

- Hypoperfusion
 - Volume depletion
 - Systemic hypotension
 - Decreased cardiac output
- Surgery
- Acidosis
- Sepsis
- Multiple organ failure
- Nephrotoxic drugs
- Pre-existing diseases

Community acquired

Radiocontrast
NSAIDs
Aminoglycosides
Colloids?

Trauma
Cardiac
Diabetes
Neoplasia
Burns

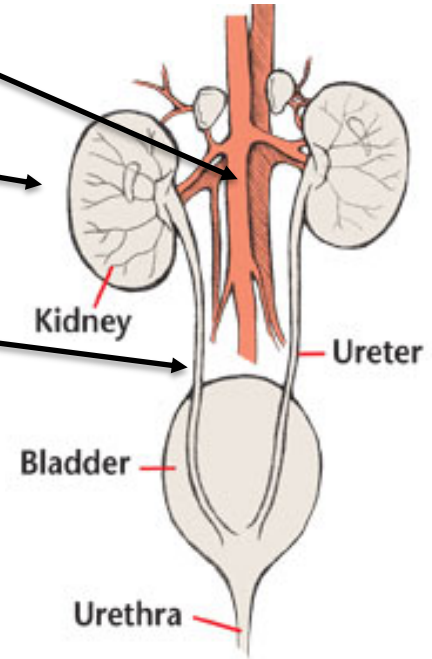
AKI



Pre-renal

Renal

Post-renal



The presence of one doesn't exclude the others!

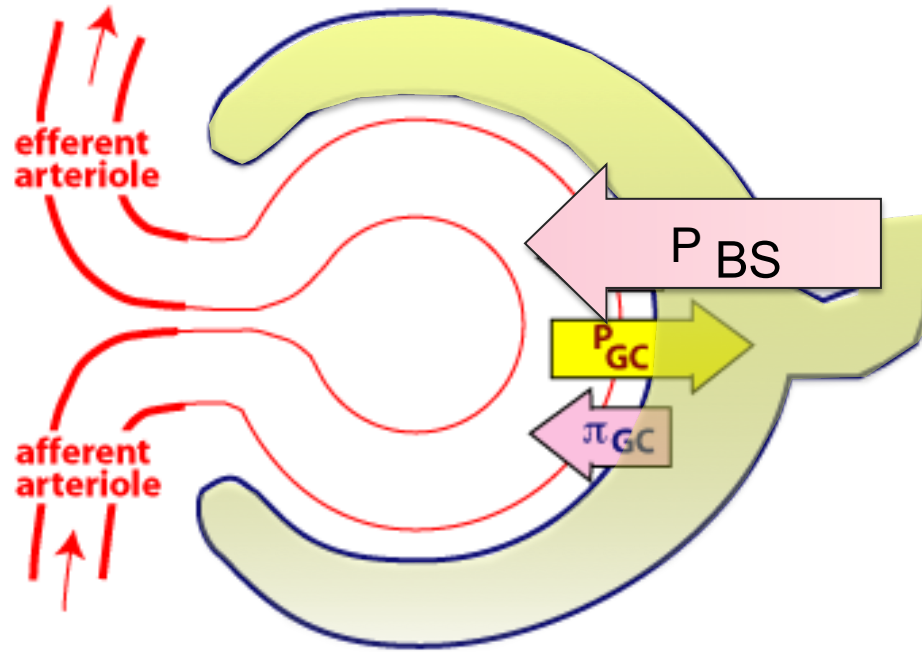
Pre- renal AKI

- Severe dehydration
- Hypovolemia
- Hypotension
- Reduced renal blood flow



Increase creatinine
Increase in USG
Reduction in UOP

Post-renal AKI



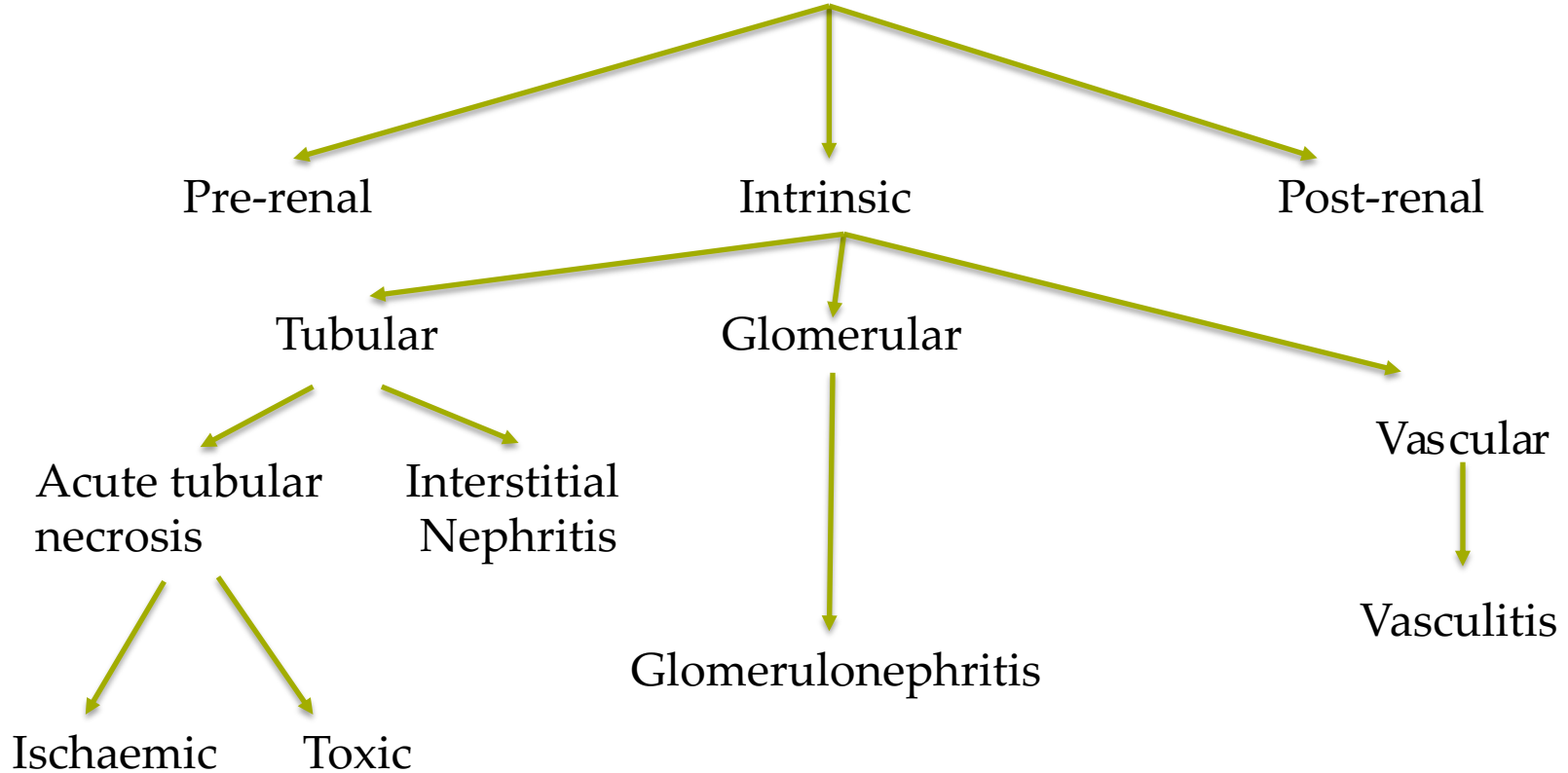
Obstruction

- Renal Pelvis
- Ureteric
- Urethral

Urinary rupture

- Bladder
- Ureters
- Urethra
- Kidneys

AKI



Early diagnosis

Particular aspects of the clinical examination:

- Hydration and perfusion status
- Anemia
- Body condition score and body weight
- Renal size, symmetry, pain
- Bladder size
- Oral ulcers
- Presence of melena
- Presence of volume overload?



Fractional excretion of Na (FE_{Na})

- May help to distinguish pre-renal to renal azotemia

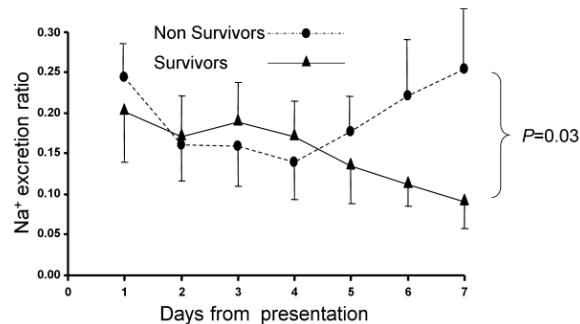
$$FE_{Na} = \frac{U_{Na} \times PCr}{P_{Na} \times UCr} \times 100$$

$FE_{Na} < 1\%$ = pre-renal

$FE_{Na} > 1\%$ = Tubular dysfunction

➤ Prognostic factor

Brown N. et al. JVIM 2015, 29: 28-34



Microbiology

- Cytology has a lower sensitivity compared to culture (even if gram stain)
- Culture always necessary
- To be interpreted in light of the sampling technique

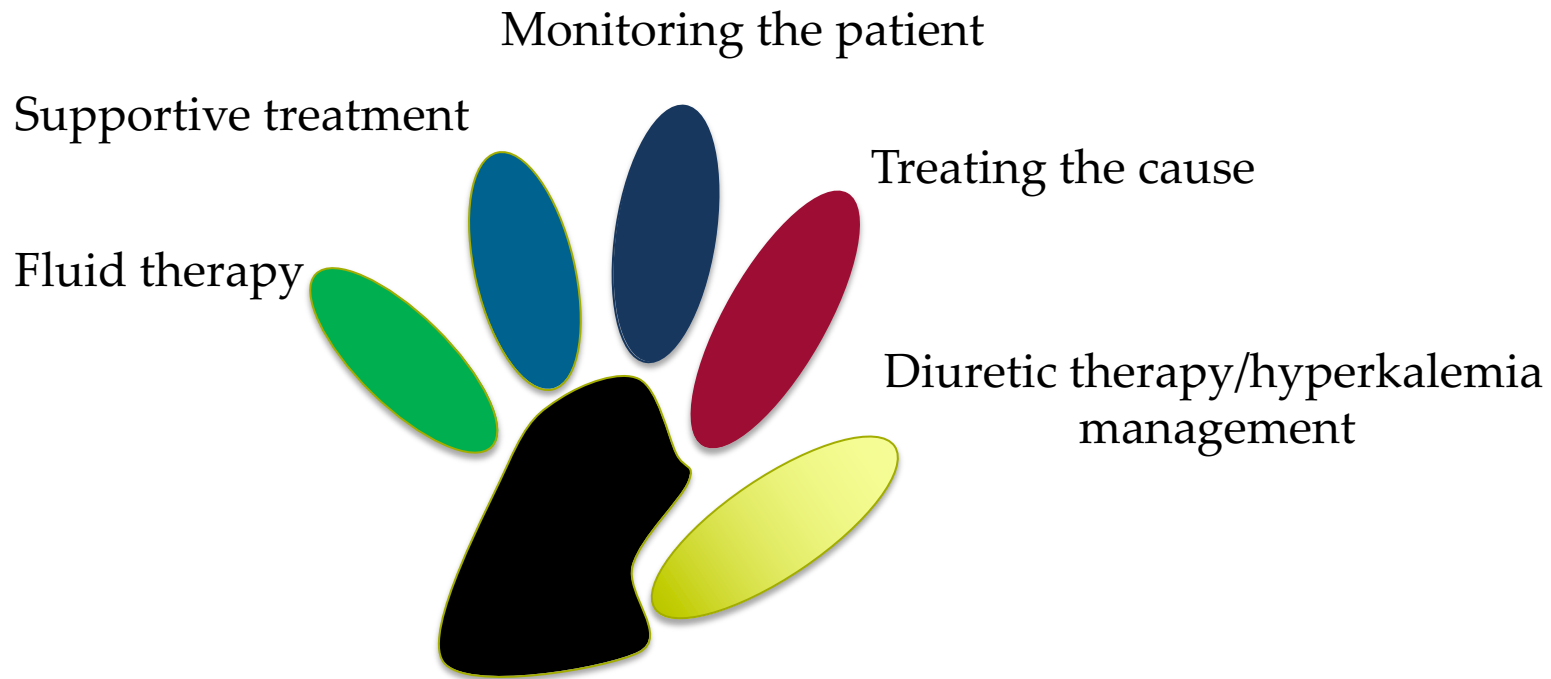
Diagnostic imaging

Abdominal ultrasound

- Abnormal structural and echogenicity abnormalities
 - Hyperechoic cortex
 - Focal masses
 - Medullary rim sign
- Possible post-renal causes

Aspirates vs Biopsies

- *FNAs* rarely diagnostic
 - Identifiable masses
 - Suspected neoplasia
- *Biopsy*
 - More useful for chronicity
 - May not provide etiological diagnosis
 - Possible complications and requires anesthesia



Fluid therapy

- Assessing the patient
 - Distinguishing between hypovolemia and dehydration
 - Calculating fluid therapy
 - Assessing outputs

Hypovolemia vs Dehydration

- Hypovolemia (loss of fluid from intravascular space)
 - May be associated with AKI
 - Clinical signs of shock
 - Perfusion parameters
 - Blood pressure
 - Plasma lactate concentration
- 
- Mentation
 - Heart rate
 - Pulse quality
 - Mucous membranes
 - Respiratory rate
 - Temperature

Fluid therapy plan

Calculating fluid therapy plan

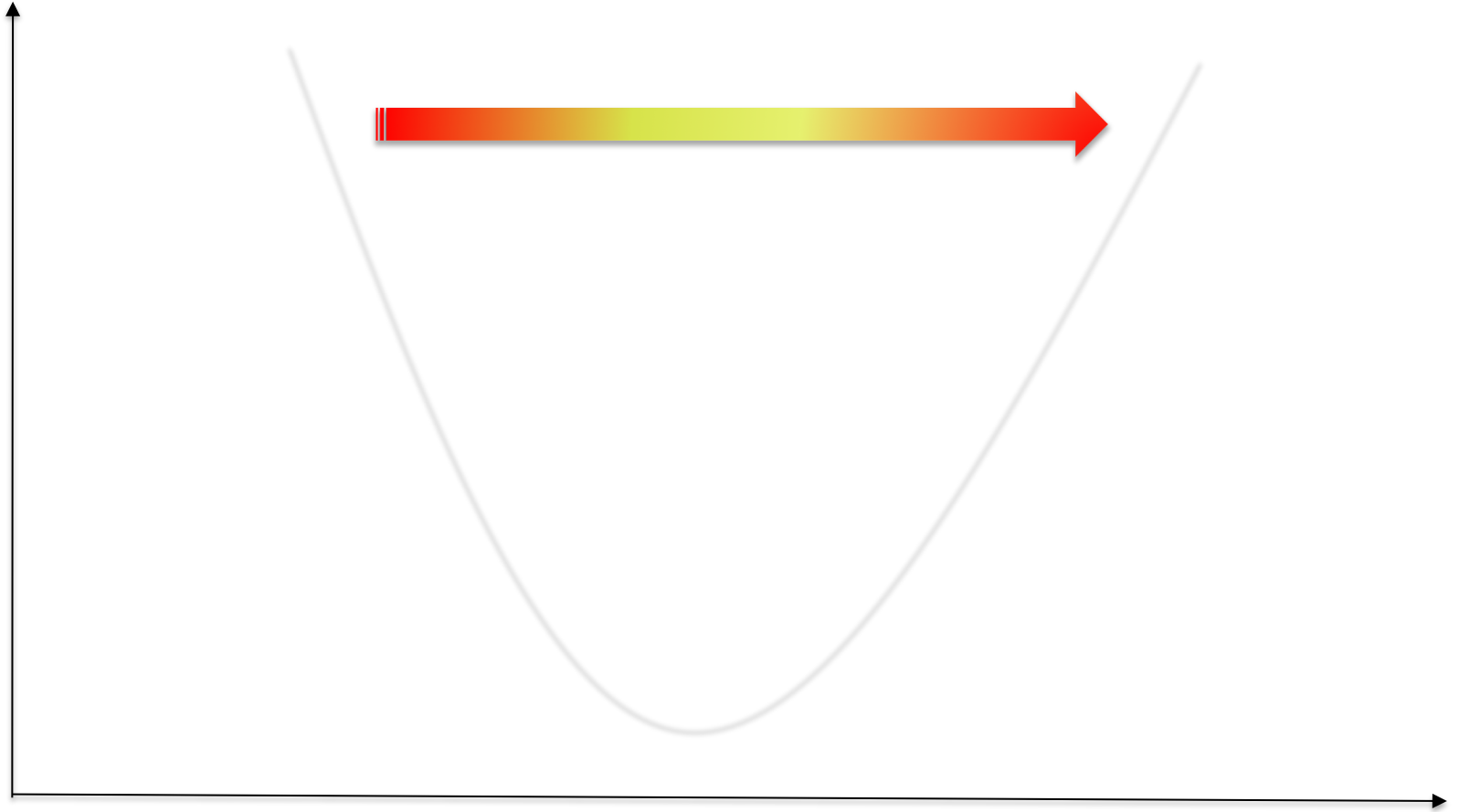
- Assessing dehydration
- Maintenance
- Ongoing losses

Maintenance phase
(ongoing hospitalisation)

Replacement phase
(12-24 hours)

Shock phase
(if present; 1 hour)

RVC



Current trend in fluid therapy

R

E
S
C
U
E

- Minutes
- Shock
- Boluses

O

P
T
I
M
I
S
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N

- Hours
- Unstable patients
- Less aggressive strategy

S

T
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B
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- Days
- Stable
- 0 fluid balance
- Minimal fluid

D

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- Days
- Stable
- Fluid reduction
- Enteral

Urine output monitoring

- Indwelling urinary catheter
- Weigh the patient q 6-8h
- Weigh inco-pads or litter tray
- Bladder monitoring q6h (palpation or ultrasound)

Essential as some patients may be anuric and other may be polyuric



Anti-hypertensive therapy

Risk category	Systolic pressure	Dyastolic pressure	Target organ damage risk
I	<150	<95	Minimal
II	150-159	95-99	Mild
III	160-179	100-119	Moderate
IV	≥180	≥120	Severe

Target organ damage secondary to hypertension

- Eye
- Heart
- Central nervous system
- **Kidney**

Consider starting anti-hypertensive treatment as soon as hypertension is detected

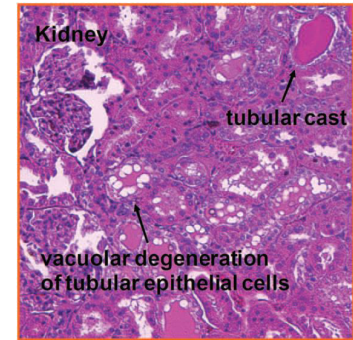
- Occurrence of hypertension in AKI on admission¹:
 - 37% (>160 mmHg) —→ 81% during hospitalization
 - 15% (>180 mmHg) —→ 62% during hospitalization
- Amlodipine
 - Starting dose 0.25 mg/kg q 24h PO
 - Can be increased progressively to 0.5 mg/kg q12h
- Hydralazine
 - 0.5-3 mg/kg q12h PO

Analgesia

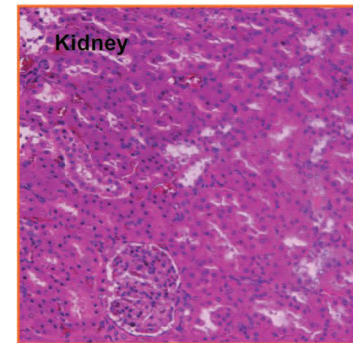
- Kidney disease may be associated with severe pain (pyelonephritis/ureteral obstruction)
- Pain score required
- Opioids
 - Buprenorphine (0.01-0.02 mg/kg IV q6-8h)
 - Methadone (0.1-0.2mg/kg IV q 4h)
- No NSAIDs

Specific treatments?

DRUGS NOT TO GIVE	DRUGS TO GIVE
NSAIDs	
Hyper-chloremic solutions	
Amikacin/Gentamicin	
Synthetic colloids	
Diuretics?	



Saline 0.9%



Balanced solution

Monitoring

- Heart rate q1-6h
- Respiratory rate q1-6h
- Temperature q12-24h
- Hydration state (free fluid check)
- Pain scoring q4-6h
- Electrolytes q 6-12h
- PCV/TS q 12-24h
- Urea-creatinine q24h
- Blood pressure q8-12h
- Fluid balance
 - (ins and outs calculation: every 24 hours; if not more frequently)
- Weight q8-12h

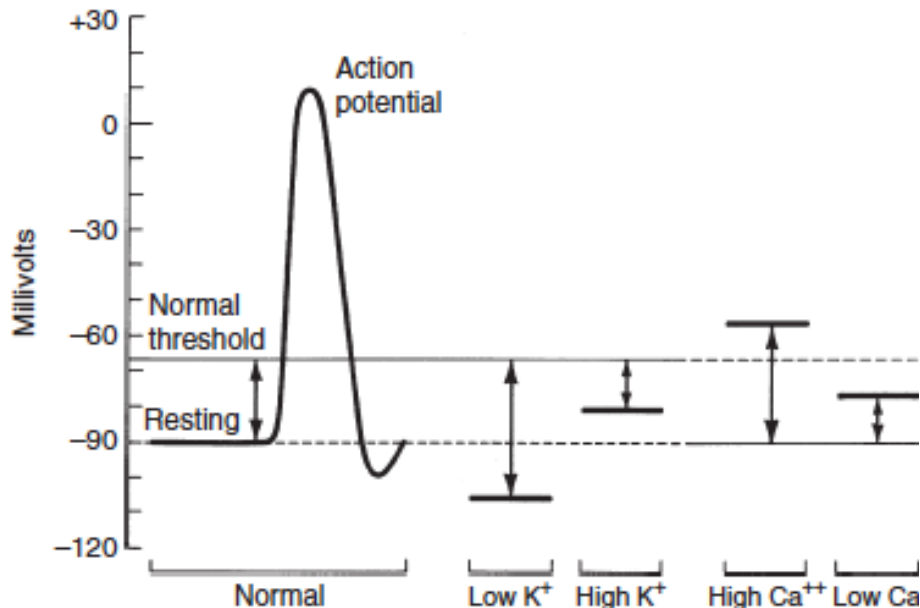


Hyperkalemia

- Caused by reduced urinary excretion of K^+
- Clinical signs mainly brady-arrhythmia

Table 51-2 Electrocardiographic Changes Secondary to Hyperkalemia¹⁴

Serum Potassium Concentration	Electrocardiographic Change
>5.5 mEq/L	Peaked, narrow T wave
>6.5 mEq/L	Prolonged QRS complex and PR interval Depressed R wave amplitude Depressed ST segment
>7 mEq/L	Depressed P wave amplitude
>8.5 mEq/L	Atrial standstill Sinoventricular rhythm
>10 mEq/L	Biphasic QRS complex Ventricular flutter Ventricular fibrillation Ventricular asystole



When to treat hyperkalemia

- High $K^+ > 7.5$ mmol/l with a non rapidly resolving condition
- Arrhythmia in the presence of hyperkalemia
- Bradycardia/ hypotension
- Hyperkalemic patient ($K^+ > 7.5$ mmol/l) undergoing anaesthesia?

Hyperkalemia treatment strategies

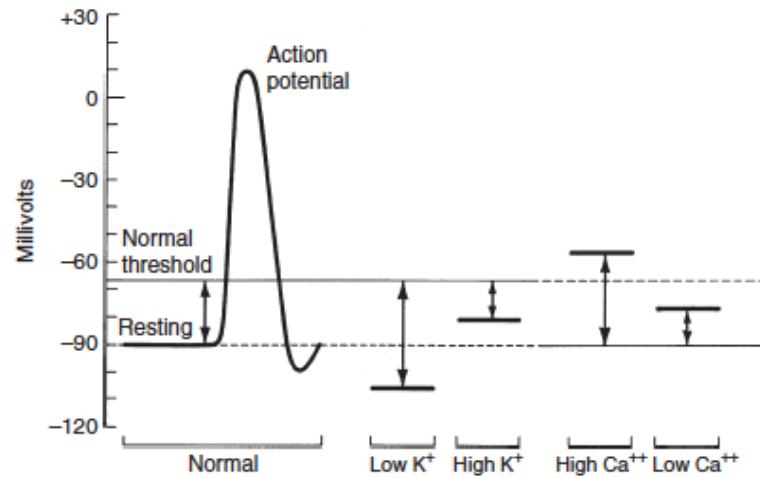
- Antagonise the effect of K^+ if **bradycardia is present**
 - Calcium gluconate
- Reduce K^+ concentration ($K^+ > 7.5 \text{ mmol/l?}$)
 - Regular Insulin
 - Sodium Bicarbonate

Table 51-3 Treatment of Life-Threatening Hyperkalemia

Drug	Dosage	Mechanism of Action	Onset of Action
10% Calcium gluconate	0.5 to 1.5 ml/kg IV slowly over 5 to 10 minutes with ECG monitoring	Increases threshold voltage but will not lower serum potassium	3 to 5 minutes
Sodium bicarbonate	1 to 2 mEq/kg IV slowly over 15 minutes	Increases extracellular pH, allowing for potassium to move intracellularly	15 minutes or longer
25% Dextrose	0.7 to 1 g/kg IV over 3 to 5 minutes	Allows for translocation of potassium into the intracellular space	<1 hour
25% Dextrose with insulin	Regular insulin at 0.5 U/kg* IV with IV dextrose at 2 g/U of insulin administered	As above	15 to 30 minutes
Terbutaline	0.01 mg/kg IV slowly	Stimulates Na^+/K^+ -ATPase to cause translocation of potassium into the cell	20 to 40 minutes

*With hypoadrenocorticism the insulin dosage should be reduced to 0.25 U/kg IV because of the patient's predisposition to hypoglycemia. ECG, Electrocardiogram; IV, intravenously; Na^+/K^+ -ATPase, sodium-potassium adenosine triphosphatase.

From "Small Animal Critical Care Medicine", Silverstein and Hopper, 2014.



Calcium Gluconate

- 0.5-1.5 ml/kg SLOWLY over 5-10 minutes
 - Risk of asystoly if administered rapidly
- Rapid onset of action (5 minutes) but temporary (30 minutes)
 - Does not reduce K^+ concentration
- Can be given twice but effect may be limited

Regular insulin

- 0.2—0.5 IU/kg IV
- 2 gr/IU_{insulin} of dextrose (dextrose 50%: 500mg/ml)
- Isotonic infusion of dextrose 2.5-5% for 6-8h
- Onset of action 15-30 minutes
- Duration variable 6-8h
- Monitor blood glucose hourly for at least 6h



Sodium Bicarbonate

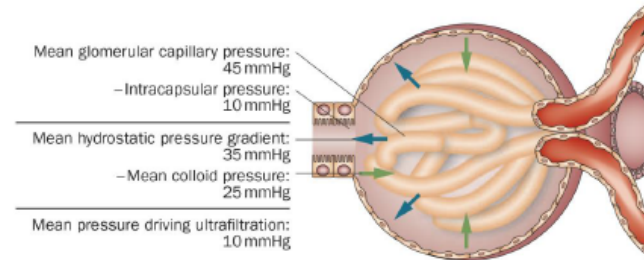
- 1-2 mEq/kg IV slowly over 20 min
- Contra-indicated in patients with respiratory depression
- May worsen hypocalcemia
- Rapid onset of action (15-30 min)
- Indicated with acidemia (pH <7.1 and severe hyperkalemia)

The patient is anuric/oliguric...

- Has any pre-renal component been treated?
- Is the hydration state adequate?
- Is the urinary catheter kinked or obstructed?

If oliguria/anuria confirmed

- Match IV fluids to UOP and other losses
- Stop IV fluids if anuric
- Do not bolus the patient



Reduced systemic pressure
Afferent vasoconstriction
Efferent vasodilation

Interstitial renal oedema
Tubular obstruction
Abnormal tubular function

Reduced renal blood flow

Low hydrostatic pressure

High intracapsular pressure

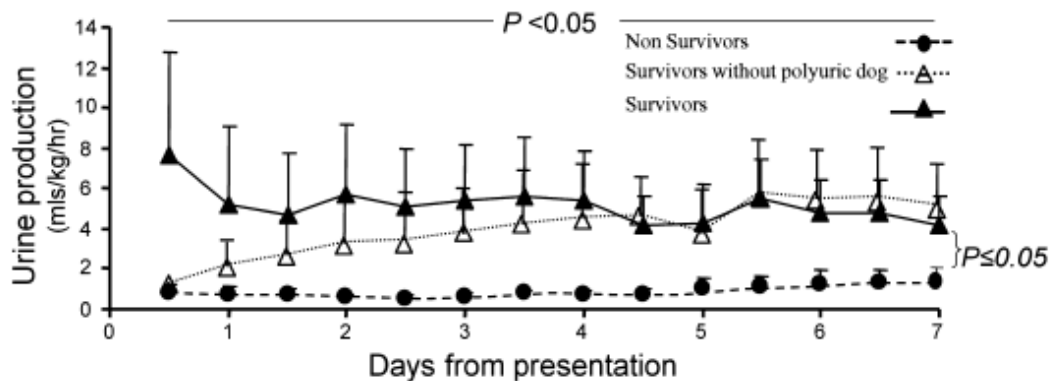
Increased oncotic pressure

Reduced G.F.R

Diuretic treatment

- Lower urine production associated with higher mortality
- Does increasing urine production improve survival?

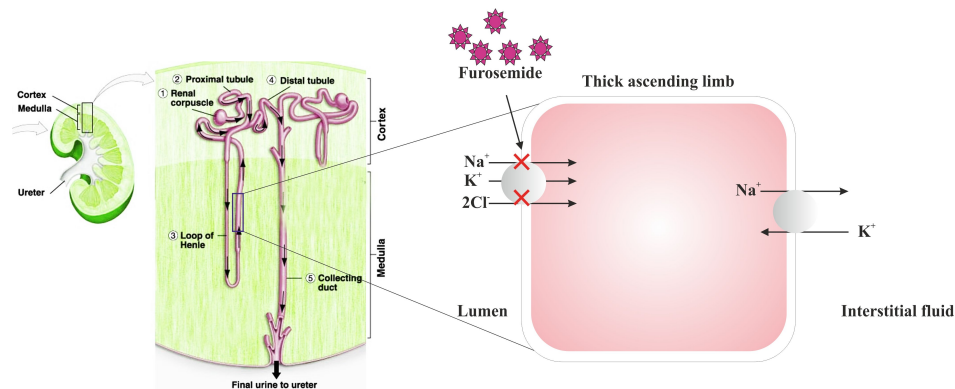
Brown et al; JVIM, 2015



Furosemide

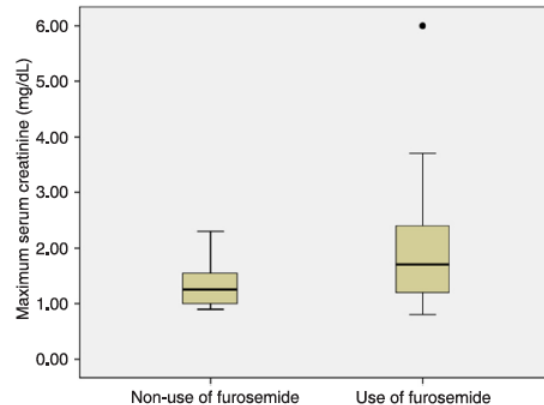
➤ Loop diuretic (action predominantly once filtered)

- Plasma effect
 - Renal afferent vasodilation
- **Tubular effect**
 - Natriuresis (0.6mg/kg dog, 1.25mg/kg cat)
 - Diuresis
 - Energy sparing effect
- Potential side effects:
 - Hyponatremia
 - Hypocalcemia
 - Hypokalemia
 - Alkalosis



Furosemide

- Not beneficial if given pre-emptively
- Increased UOP $\neq$ increased GFR
- In people, its use may be associated with increased incidence of AKI
- Do not use while giving fluids



Furosemide

Indications:

- Oliguria (0.5 ml/kg/h)
 - Not necessary if normovolemic
- Anuria
- Hypervolemic patient

Bolus or constant rate infusion?

1-2 mg/kg followed by 0.1-1 mg/kg/h C.R.I

Table 1: Urine output following furosemide administration

			Time (h)				
Baseline			1	2	4	6	8
Hourly urinary output (mL/h)	IV	16.3	260.5*	60.0	12.6	14.0	8.2
		[5.9–62.8]	[191.5–430.0]	[19.2–83.5]	[8.5–132.0]	[7.4–36.6]	[5.4–30.1]
	SC	12.0	242.0*	96.0*	26.0	13.0	8.2
		[10.0–38.0]	[136.0–381.0]	[66.5–169.4]	[12.0–44.9]	[6.6–24.6]	[5.8–16.0]
	PO	12.5	63.8	98.2*	108.4*	32.5	13.4
Accumulated urinary output (mL)	IV	[9.0–55.0]	[18.0–144.0]	[18.0–169.0]	[39.6–220.0]	[10.1–56.0]	[7.4–43.5]
		CRI	12.6	103.9	136.0*	146.8*	93.0*
	IV	[8.0–40.0]	[50.0–194.0]	[113.0–274.5]	[103.8–357.8]	[62.8–180.5]	[55.0–182.0]
		SC	28.3	275.8	335.9	348.5	355.9
	PO	[1.0–31.3]	[207.8–486.0]	[227.0–558.0]	[238.5–690.0]	[247.4–726.6]	[262.4–756.7]
Accumulated urinary output (mL)	SC	28.3	280.0	376.0	391.9	400.4	411.4
		[25.3–31.3]	[148.6–405.8]	[264.4–575.2]	[309.3–607.2]	[320.9–630.2]	[326.7–646.2]
	PO	28.3	76.7	174.5	307.3	355.9	378.1
		[25.3–31.3]	[34.8–156.5]	[103.3–250.8]	[178.3–403.8]	[188.4–450.8]	[195.8–459.4]
	CRI	28.3	119.7	273.9	443.5	534.0	608.7
		[25.3–31.3]	[62.6–234.0]	[222.7–386.9]	[326.5–744.7]	[389.3–925.2]	[446.3–1107.2]

Adin et al. JVIM 2003; 17: 632-636

Mannitol

Osmotic diuretic

- Urinary flow improvement (61%)
- Renal blood flow improvement and reduction of renal vascular resistance
- Reduction of the tubular oedema

Only indication:

- Oliguria (0.5 gr/kg and evaluate response)

Contraindicated in

- Anuric patients
- Volume overloaded patients

Other diuretics: Dopamine

- Dopaminergic receptor effect (DA-1/DA2)
- Alpha₂ effect in cats?
- Low doses 0.5-3 µg/kg/min
- Possible improvement in renal blood flow and urinary output
- No improvement in survival in people with AKI
- Associated with adverse effects in clinical and experimental studies
- **Cannot be justified in the treatment of AKI**

Other diuretics

Fenoldopam

- Selective DA-1 agonist (used as CRI)
- Shown to increase UOP in healthy cats and GFR in dogs (Simmons et al, 2006; Halpenny et al, 2001; Kelly et al, 2016)
- A retrospective study has not shown any benefit in its use in AKI in dogs and cats (Nielsen et al, 2015)

Diltiazem

- Ca⁺-channel blocker/ reduction in renal vasoconstriction
- No improvement observed in dogs with leptospirosis (Mathews et al, 2007)

Polyuria

- Following the anuric-oliguric phase, a variable polyuric phase occurs
- Can last days/weeks
- May be severe (4-10ml/kg/h)
- If unmatched
 - Dehydration
 - Worsening azotemia (despite improvement)
 - Electrolyte disorders (hypokalemia/hyponatremia)
- Once creatinine and UOP plateaus start reducing fluid therapy by 20% daily

What if there is no improvement?
Any other option?

Renal replacement therapy

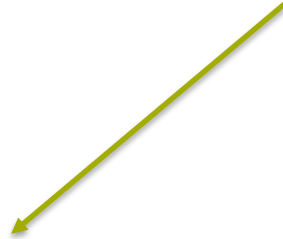
- Therapy that replaces the normal blood-filtering function of the kidneys
 - Electrolyte and acid-base balance
 - Fluid balance
 - Removes waste- toxins
- Does not fix the kidney
- It allows to treat life-threatening conditions for few days/weeks awaiting for the kidney to regain its function

Acute kidney injury

Anuric/oliguric; non responsive to medical

management

Hyperkalemia



Volume overload
AKI refractory to diuretics

Toxins

Removing toxins from the
circulation (ethylene glycol)

Severe azotemia and acidosis



Renal Replacement Therapy

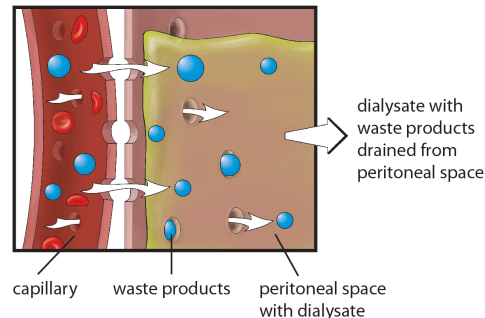
- Peritoneal Dialysis
 - Use of the peritoneum as a filter
- Extracorporeal RRT
 - Intermittent
 - Short cycle (3-4h) used to treat patients with acute and chronic kidney disease
 - Very efficient
 - Continuous
 - Longer cycle (24h) to reduce azotemia, hyperkalemia and remove excessive fluid
 - Prolonged intermittent
 - Cycle of 8-12 hours to improve efficiency, patient safety and need for staff

Peritoneal Dialysis

- Requires an abdominal drain
- Infusion of a sterile solution in the abdomen
- Dwell time of 30-40 minutes
- Removal of the abdominal fluid (and diffused solutes and electrolytes, including urea, creatinine and potassium)
- Repeated cyclically every 2 h or as needed



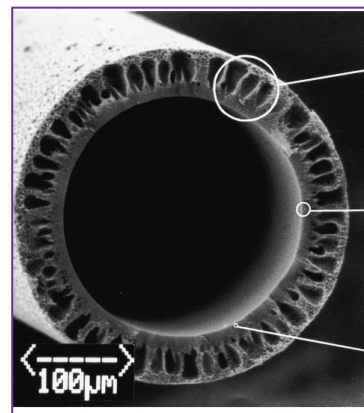
waste products cross the semipermeable membranes into the peritoneal space



Extracorporeal Renal Replacement Therapy

Blood is continuously drawn through a catheter from the patient into a filter and reinfused in the patient

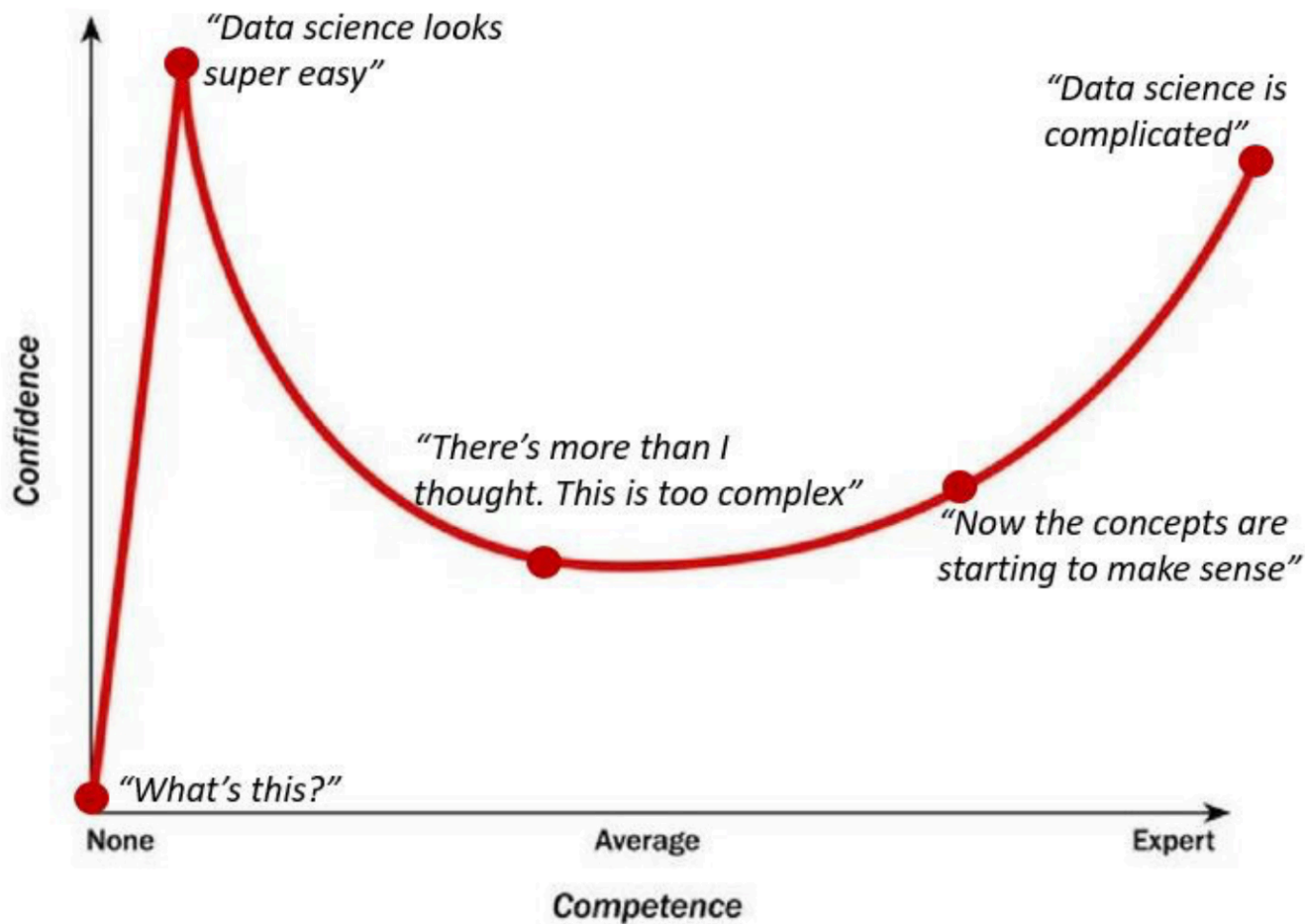




Prognosis

- Variable
- 53% mortality in dogs and 45% in cats
 - 19% mortality for infectious causes
 - 56% mortality for non-infectious causes
- 50% of these may remain azotemic
- Leptospirosis better outcome (82% survival)

Dunning-Kruger effect in Data science



Questions?

13.15 – 14.30

Ventilation in the ICU in small animals

(S. Cortellini)

Mechanical ventilation in intensive care

Stefano Cortellini

DMV, MVetMed, Dipl.ACVECC, Dipl.ECVECC, FHEA, MRCVS

Lecturer in Emergency and Critical Care

scortellini@rvc.ac.uk

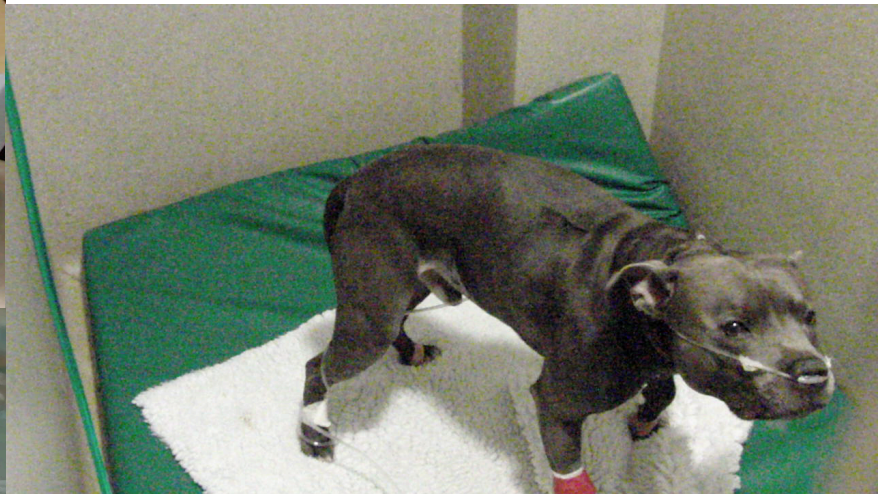
- Indications: are we changing our approach?
- Why is it different?
- Methods of ventilation
 - Ventilatory strategies/modalities
 - Recruitment maneuvers
 - Weaning
- Management of the ventilated patient...time for protocol

Why is it different

- Length of anesthesia
- Patient characteristic
 - Respiratory dysfunction
 - Cardiovascular instability
 - Co-morbidities
- Long term management

Indications for mechanical ventilation

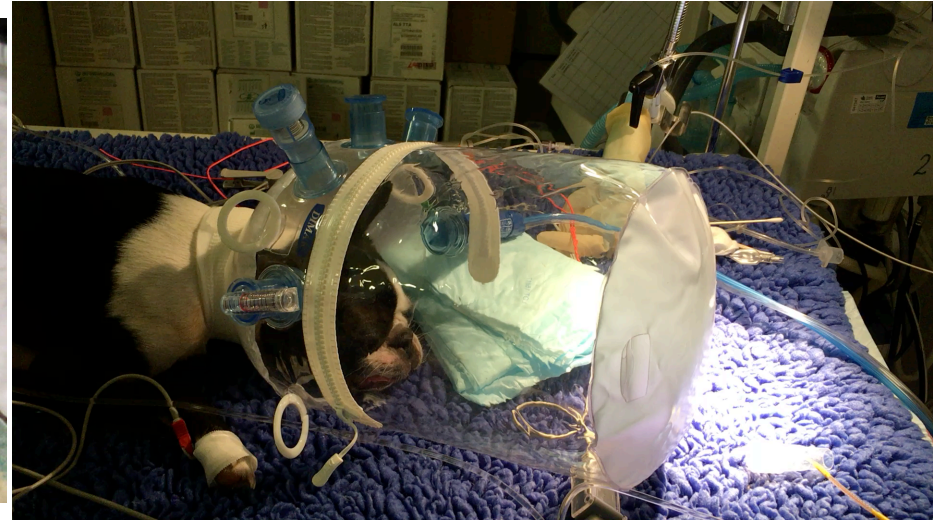
- PaO_2 : < 60 mmHg
- $\text{PaCO}_2 > 50$ mmHg
- Signs of respiratory fatigue
- Moving towards other indications..
 - Decreasing work of breathing and oxygen consumption
 - Recovery from anesthesia



Any additional tools we have before starting mechanical ventilation?



High Flow Nasal Cannula Oxygen
(HFNC)



Continuous Positive Airway Pressure
(CPAP)

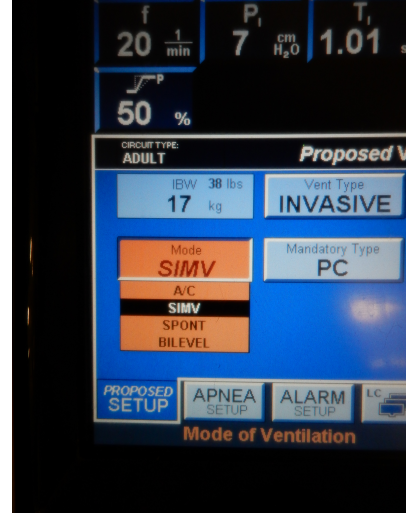
Type of ventilators: what are we looking at?

- Different modes
 - Synchronization
 - Lung protective strategy
 - Weaning



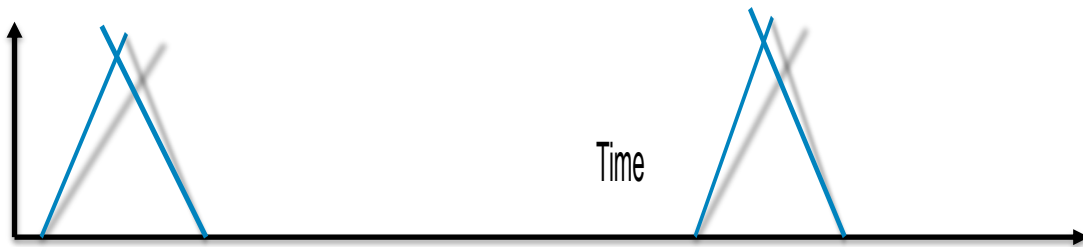
Modes of ventilation

- Assisted Control (A/C)
- Synchronized Intermittent Mandatory Ventilation (SIMV)
- Pressure Support (PS)

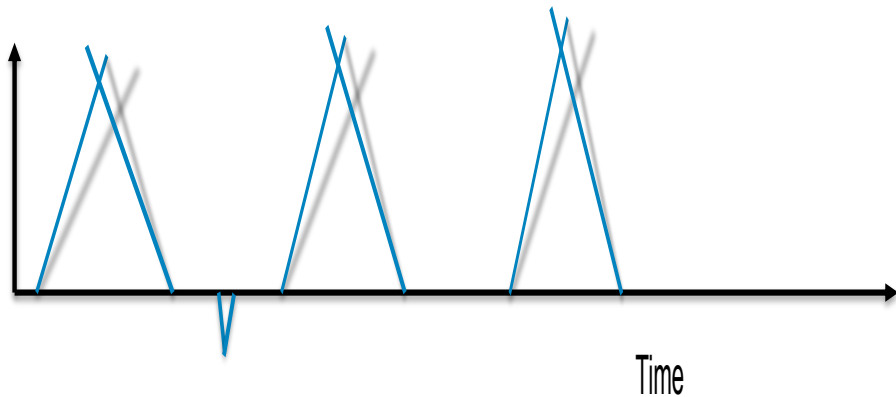


Assisted Control

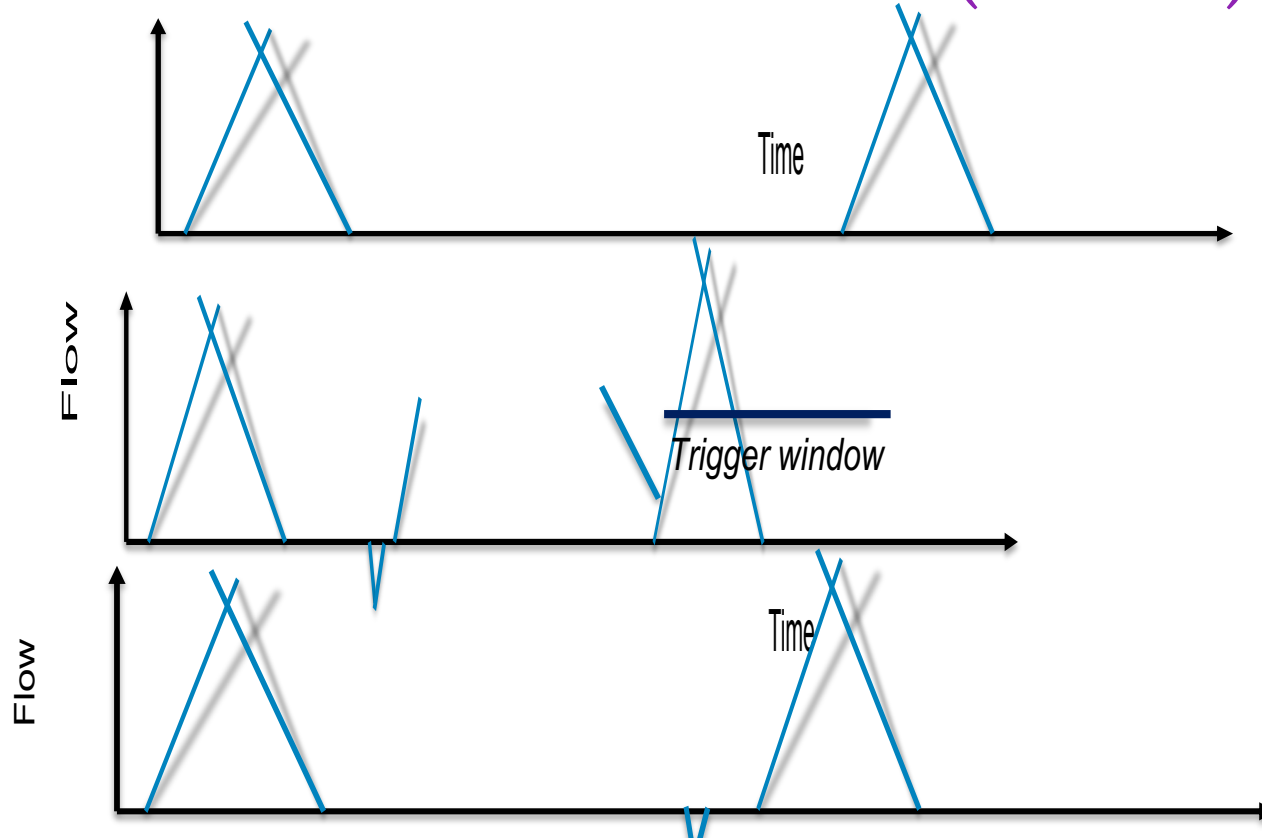
Flow



Flow



Synchronised Intermittent Mandatory Ventilation (SIMV)



Modes of ventilation

Pressure-controlled

- Advantage: Peak Inspiratory Pressure and Peak Alveolar Pressure remain constant
- Disadvantage: V_T varies according to patient's demand/ characteristics
(compliance/resistance)

Volume-controlled

- Advantage: Constant level of alveolar ventilation
- Disadvantage: potential asynchrony (due to fixed flow pattern) and lower compliance

Mode of ventilation: philosophy

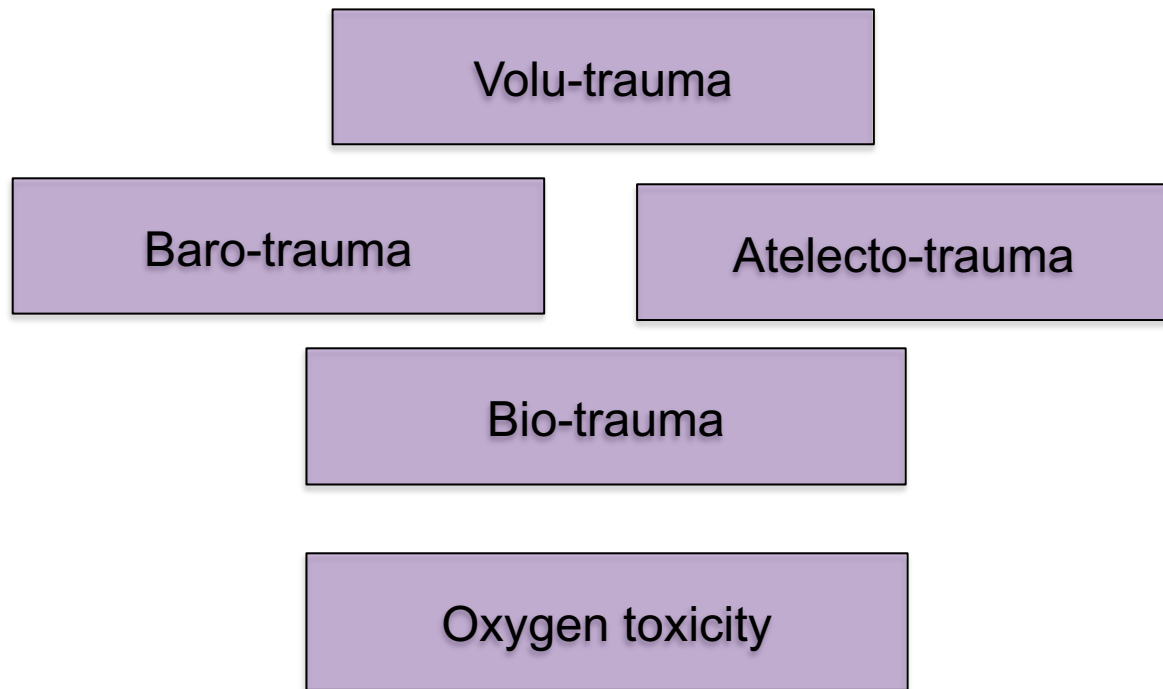
➤ Open Lung theory



➤ Baby Lung ventilation

- Residual portion of lung maintaining normal aeration during ARDS
- Very small amount of normal lung (hence “baby lung”)

Ventilator Associated Lung Injury (VALI)



So what does this mean?

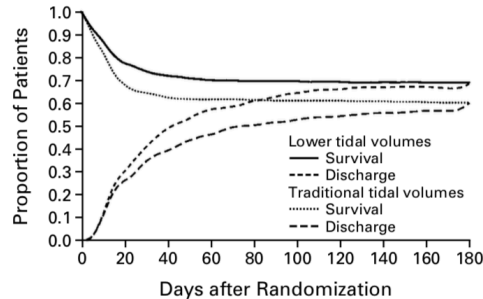
Initial theory

- Low tidal volume
- Using Positive End Expiratory Pressure (PEEP)
- Limiting peak pressures

Low tidal volumes: why?

TABLE 3. RESPIRATORY VALUES DURING THE FIRST SEVEN DAYS OF TREATMENT IN PATIENTS WITH ACUTE LUNG INJURY AND THE ACUTE RESPIRATORY DISTRESS SYNDROME.*

VARIABLE	Day 1		Day 3		Day 7	
	GROUP RECEIVING LOWER TIDAL VOLUMES	GROUP RECEIVING TRADITIONAL TIDAL VOLUMES	GROUP RECEIVING LOWER TIDAL VOLUMES	GROUP RECEIVING TRADITIONAL TIDAL VOLUMES	GROUP RECEIVING LOWER TIDAL VOLUMES	GROUP RECEIVING TRADITIONAL TIDAL VOLUMES
Tidal volume (ml/kg of predicted body weight)	6.2±0.9	11.8±0.8	6.2±1.1	11.8±0.8	6.5±1.4	11.4±1.4
No. of patients	387	405	294	307	181	179
Plateau pressure (cm of water)	25±7	33±9	26±7	34±9	26±7	37±9
No. of patients	384	399	294	307	168	173
Peak inspiratory pressure (cm of water)	32±8	39±10	33±9	40±10	33±9	44±10
No. of patients	382	401	295	308	178	177
Mean airway pressure (cm of water)	17±13	17±12	17±14	19±17	17±14	20±10
No. of patients	369	385	288	301	176	173
Respiratory rate (breaths/min)	29±7	16±6	30±7	17±7	30±7	20±7
No. of patients	389	406	296	308	185	181
Minute ventilation (liters/min)	12.9±3.6	12.6±4.5	13.4±3.5	13.4±4.8	13.7±3.8	14.9±5.3
No. of patients	387	401	296	307	182	177
FiO ₂	0.56±0.19	0.51±0.17	0.54±0.18	0.51±0.18	0.50±0.17	0.54±0.20
No. of patients	390	406	296	308	185	181
PEEP (cm of water)	9.4±3.6	8.6±3.6	9.2±3.6	8.6±4.2	8.1±3.4	9.1±4.2
No. of patients	390	406	296	308	185	181



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VENTILATION WITH LOWER TIDAL VOLUMES AS COMPARED WITH TRADITIONAL TIDAL VOLUMES FOR ACUTE LUNG INJURY AND THE ACUTE RESPIRATORY DISTRESS SYNDROME

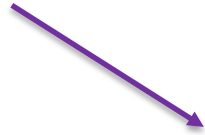
THE ACUTE RESPIRATORY DISTRESS SYNDROME NETWORK*

TABLE 4. MAIN OUTCOME VARIABLES.*

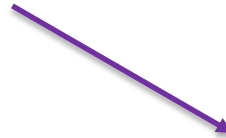
VARIABLE	GROUP RECEIVING LOWER TIDAL VOLUMES	GROUP RECEIVING TRADITIONAL TIDAL VOLUMES	P VALUE
Death before discharge home and breathing without assistance (%)	31.0	39.8	0.007
Breathing without assistance by day 28 (%)	65.7	55.0	<0.001
No. of ventilator-free days, days 1 to 28	12±11	10±11	0.007
Barotrauma, days 1 to 28 (%)	10	11	0.43
No. of days without failure of nonpulmonary organs or systems, days 1 to 28	15±11	12±11	0.006

Low tidal volumes: why?

Overdistension



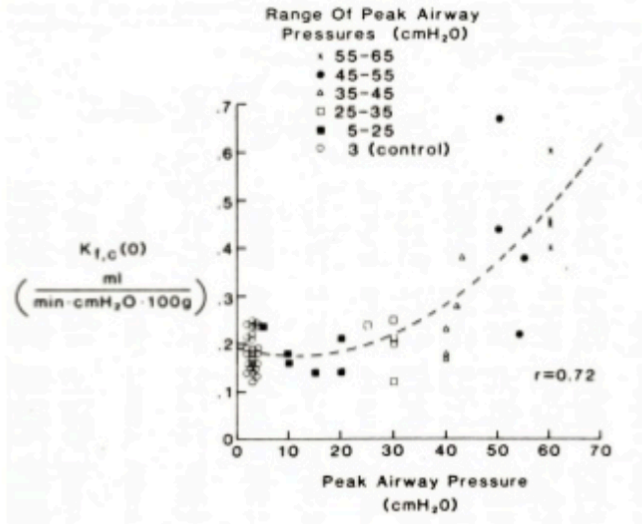
Volutrauma



Excessive strain

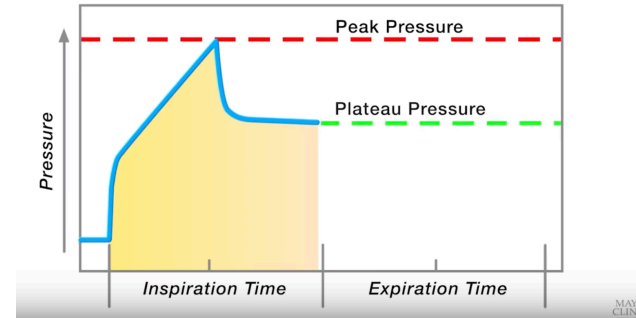
Limiting pressures: why?

Peak pressures

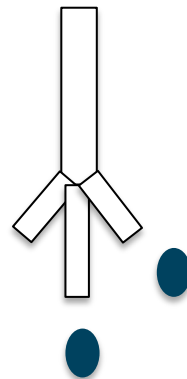


Parker et al, 1984

Plateau pressures



PEEP: why?



Increase in Functional
Residual Capacity



Improvement of
oxygenation

Reduction of alveolar
collapse-distension



Reduction of
biotrauma

What are the current mechanical ventilation in veterinary medicine?

Targets

- Normoxemia
 - PaO_2 60-80 mmHg
 - SpO_2 88-92/96%
 - Avoid oxygen toxicity
- Permissive hypercapnia
- Aim at gentle settings

Parameter	Normal Lung	Diseased Lung
FiO_2	100%	100% (aim as low as you can)
Tidal Volume (ml/kg)	8-12	6-8
Resp. rate	10-20	15-30
Minute ventilation (ml/kg)	150-250	100-250
PEEP (cm H_2O)	0-4	4-8
Pressure above PEEP	8-10	10-15
Inspiratory-to-expiratory ratio	1:2	1:1 to 1:2

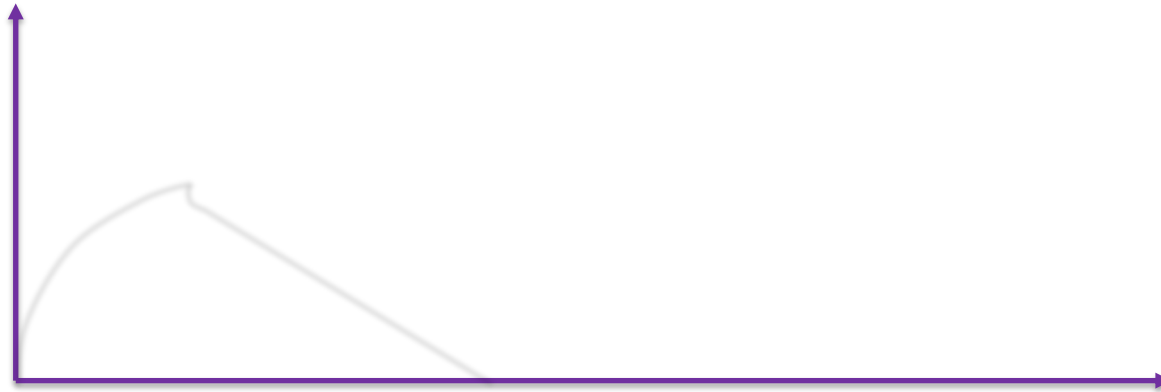
What is the problem with this approach?

- PEEP in diseased lung
 - May predispose to overdistension
 - Increase in static strain
 - Reduced lymphatic drainage
 - Reduced cardiac output
- Is the PEEP always associated with improved outcome?

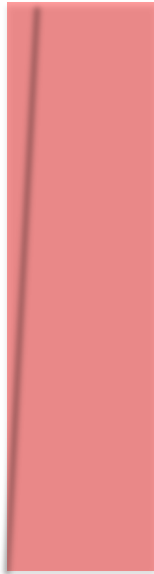
Forces that damage the lungs

Stress: force per unit area

Strain: the change in length in relation to the initial length



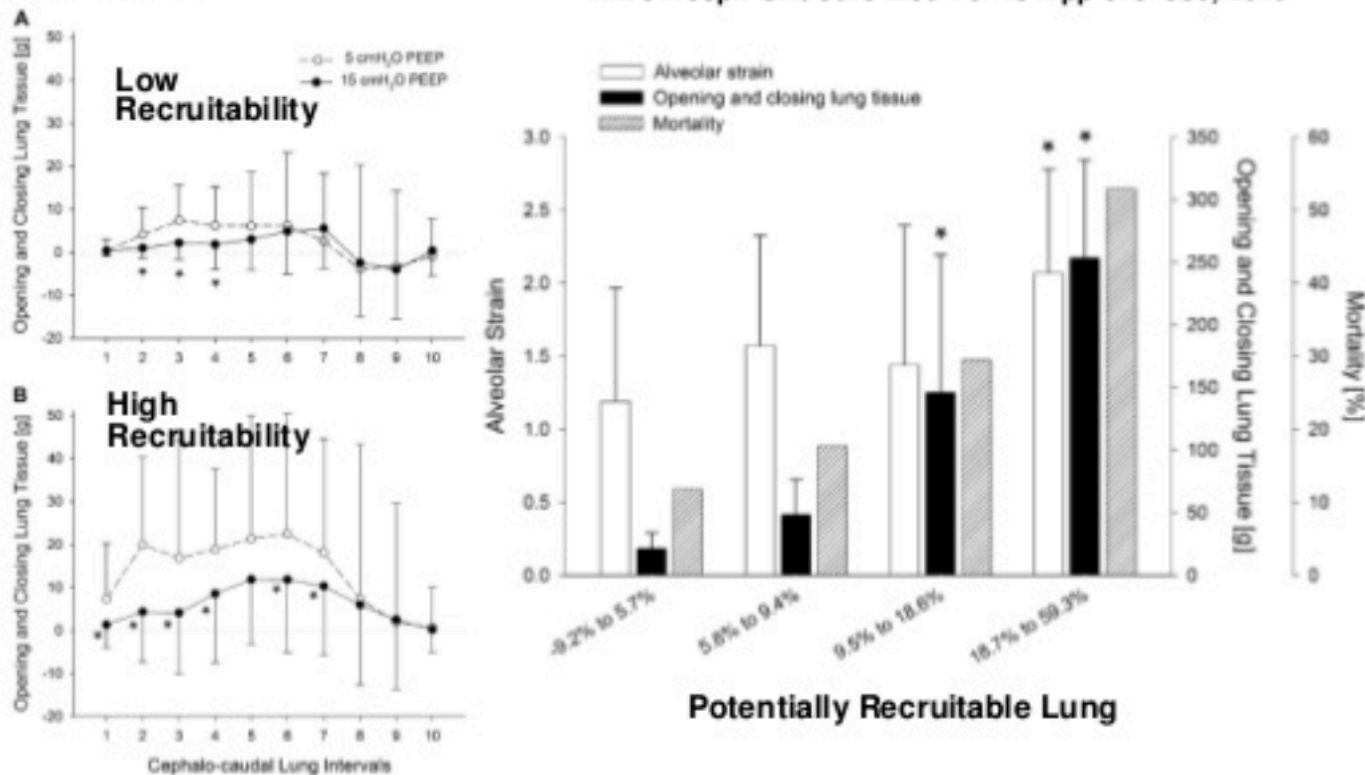
Dynamic strain vs static strain



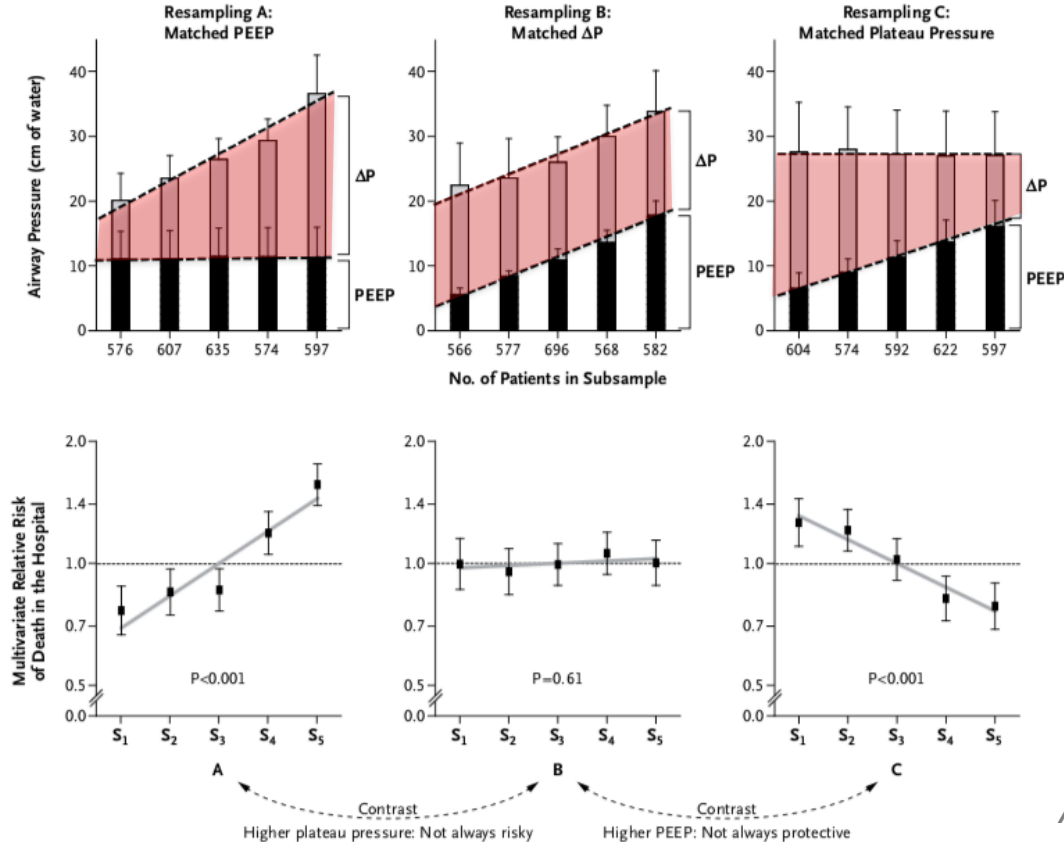
Lung Opening and Closing during Ventilation of Acute Respiratory Distress Syndrome

Pietro Caironi^{1,2}, Massimo Cressoni¹, Davide Chiumello², Marco Ranieri³, Michael Quintel⁴, Sebastiano G. Russo⁴, Rodrigo Comejo⁵, Guillermo Bugedo⁵, Eleonora Carlesso¹, Riccarda Russo², Luisa Caspani², and Luciano Gattinoni^{1,2}

Am J Respir Crit Care Med Vol 181. pp 578–586, 2010

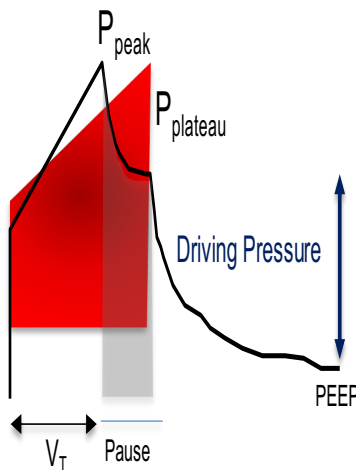


Driving pressure



Driving pressure

- Difference between Plateau Pressure and PEEP in patient with no spontaneous breathing
- Should be 12-15 cmH₂O
- Cause in strain-stress



How does this change our approach

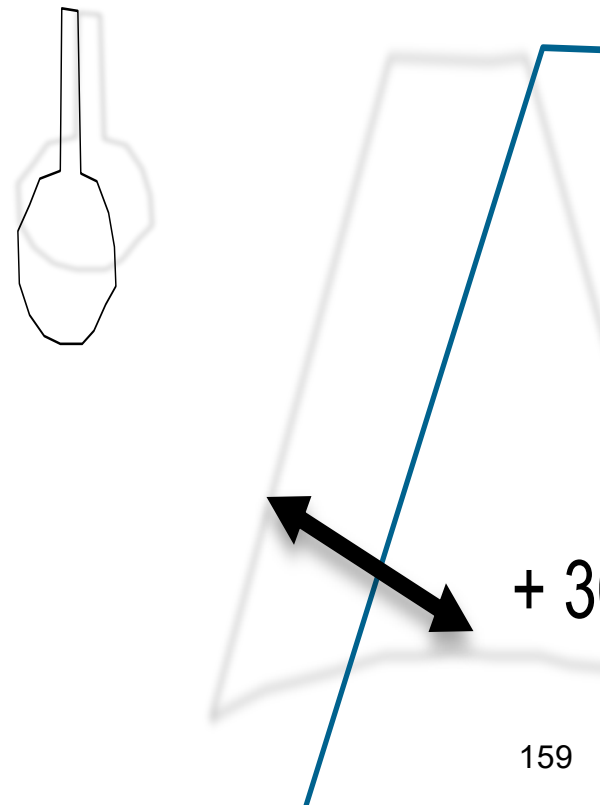
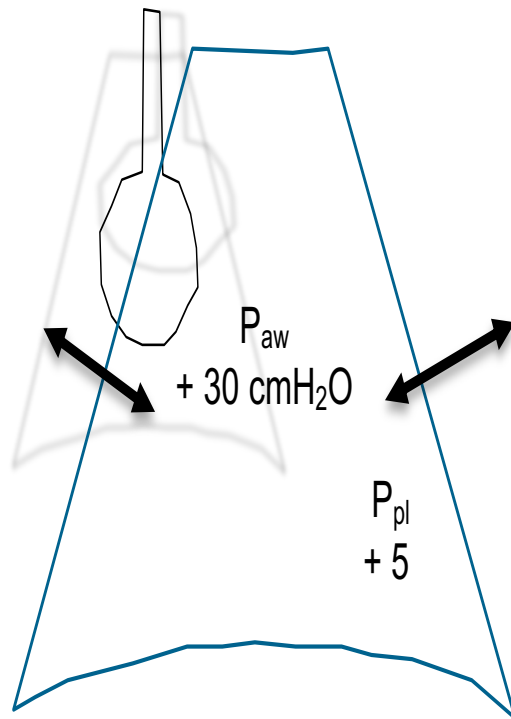
How does this change our approach..

- Minimize alveolar overdistension
 - $P_{\text{plat}} < 30 \text{ cmH}_2\text{O}$ or $V_T < 7 \text{ ml/kg}$
- Minimize alveolar decruitment during expiration
 - PEPP moderate
- Decrease transpulmonary cycling pressure
- Consider neuromuscular blockers?

Neuromuscular agents

- Indications:
 - Refractory hypoxemia
 - Facilitation of mechanical ventilation
 - Patient/ventilatory asynchrony
- Surviving sepsis campaign:
 - Use of NMBA short-course with $\text{PaO}_2:\text{FiO}_2 < 150$
- Drugs:
 - Atracurium
 - Laudanosine metabolite: neurological toxicity
 - Pancuronium





Neuromuscular blocking agents

- Reversible muscle paralysis
- More effective in early phases:
 - Decreased thoraco-pulmonary compliance
 - Increase in functional residual capacity
 - Reduced transpulmonary pressure
 - Reduced lung strains
- NMBA vs placebo:
 - Reduction of PEEP/plateau pressures
 - Improvement of PaO_2 and $\text{PaO}_2/\text{FiO}_2$ in the first 48 to 120 hours
 - Reduction of ventilator-free days
 - Reduction of mortality in patients with ARDS

1. Papazian et al; NEJM, 2010
2. Gainnier et al; Crit Care Med, 2004
3. Forel et al; Critic. Care med 2006

Problems with translating human guidelines to small animals



Recruitment manouvers: are they really necessary?

- Transient increases in trans-pulmonary pressures to open up atelectasis alveoli
- Part of the “*Open Lung approach*”
- Reduces the collapsed lungs and cyclic de-recruitment

Recruitment strategies
40cmH ₂ O for 40-60 seconds
3 consecutive sighs/min with a plateau pressure of 45 cmH ₂ O
2 minutes of peak pressure of 50 cmH ₂ O and PEEP above upper inflection point

Weaning: when to consider discontinuing ventilation

- Indication for MV has resolved/is improving
- Adequate gas exchange without positive pressure ventilation
- Stable on the cardiovascular side
- No excessive secretions (potential occlusion)
- Neurologically normal
- Specific targets
 - Oxygenation adequate:
 - With reasonable FiO_2
 - No PEEP
 - Gentle ventilatory settings
 - Adequate ventilation

Weaning methods



Management of ventilator patient: don't just look at the respiratory system...



20 Kirby's rule

Fluid balance	GI motility
Oxygenation and ventilation	Nutrition
Blood pressure	Renal function
Heart rate/contractility/rhythm	Coagulation
Glucose	Immune status/antibiotics/infections
Body temperature	Drug dosage and metabolism
Albumin	Wound care and bandages
Electrolytes	Analgesia
CNS/mentation	Nursing care
RBCs and hemoglobins	Tender loving care

Fluid status

- Monitor urinary output
- Can have reduced UOP:
 - Reduced cardiac output
 - Increase in ADH release
 - Increased intrathoracic pressure
 - Opioid administration
 - Decrease in ANP release
- Consider furosemide low dose to improve diuresis if necessary

Ventilator Associated Pneumonia: the silent killer

- Barrier Nurse
 - Always use disposable or sterile gloves
 - Intubate with sterile ET tube
 - Suction with sterile tube
 - Oral care
- Adequate (and appropriate!) use of antibiotics
- Subglottid suction?

14.30 – 15.15

Fluid therapy and resuscitation in foals

(E. Paulussen)

Fluid therapy and resuscitation in equine neonates

Ellen Paulussen, DVM, Dipl. ECEIM

One of the main dilemmas when evaluating a sick neonatal foal is whether or not fluid therapy is indicated. One must consider the variety of indications for fluid therapy, the different types of fluid, different routes of administration, the amount of fluid and the anticipated duration of the therapy.

Patient requirement for fluid therapy

The first challenge in patient evaluation is the accurate assessment of hydration status. The typical parameters used are mucous membrane color, capillary refill time, jugular refill time, pulse quality, temperature of the extremities, mental status and urine production. Fundamentally these are indicators of perfusion, rather than hydration, which is an important distinction given that there are situations, such as cardiogenic or vasodilatory shock, in which a well-hydrated patient can present extremely poor perfusion. The clinical signs most commonly used for the assessment of hydration are increased skin turgor (although not reliable in foals), tacky mucous membranes and sunken eyes. Further insights into hydration status can be gained by the measurement of urine specific gravity. Values of greater than 1.010 indicate that the foal is retaining water and is likely not adequately hydrated. Urine output is another useful parameter, but it can be hard to gauge in foals that are not continuously monitored. The normal foal urinates at least once every 2 hours. Hypotension, considered a mean arterial pressure less than 60 mmHg, may be an indication of hypovolemia but can also result from decreased cardiac output or excessive venous capacitance.

Types of fluid

There are many choices of fluids and they fall into three broad categories: crystalloids, colloids and oxygen-carrying solutions. Crystalloid solutions contain electrolytes and nonelectrolytes (such as dextrose) that are capable of diffusing through the capillary wall into the interstitium, whereas colloid solutions contain larger molecules that do not readily diffuse and tend to remain within the vascular lumen. Oxygen-carrying solutions contain either red blood cells or other substances capable of delivering oxygen from the lungs to the tissues. In the majority of situations the most appropriate fluid will be a crystalloid solution. These solutions are classified based on their tonicity relative to normal plasma. Isotonic fluids will expand the ECF volume, expanding the circulating blood volume. Because these fluids contain large amounts of sodium they can result in hypernatremia, which has been associated with increased mortality and severity of illness in human patients. Hypotonic crystalloid solutions contain much less sodium and chloride, this can be very helpful because the lower sodium load decreases the risk of water retention and edema formation, and the lower chloride load decreases the risk of hyperchloremic metabolic acidosis. For this reasons hypotonic solutions are most useful for maintenance fluid therapy, in which there is less need for electrolyte replacement and more need for the provision of water. Hypertonic crystalloid fluids have higher electrolyte concentrations than plasma and have fewer indications for their use. The most commonly used hypertonic solution is hypertonic saline (NaCl 7.2%), which is primarily used to expand the circulating blood volume.

Route of administration

The most physiologic route of fluid administration is the enteral route, but it can be easy to overlook the utility of this route, especially in hospitalized patients. Generally, if the gut is working it should be used for at least whatever component of the fluid therapy is appropriate. IV administration will achieve the most rapid result because it allows for a large amount of fluid to be given, but IV access is associated with some complications such as thrombophlebitis and air embolism aspiration. Neither

subcutaneous nor intraperitoneal fluid administration is well tolerated in equine patients and these routes are rarely used.

Dosage

The factors that must be considered in determining the amount of fluids to administer are the volume needed for maintenance of normal body function, the magnitude of the existing fluid deficit and the ongoing losses potentially associated with the disease process (diarrhea, reflux, sweat). When designing the fluid therapy plan it is important to consider the maintenance fluid as separate from the replacement fluid plan, which includes both replacement of existing deficits and ongoing losses.

The calculation of **maintenance fluid** requirements in the foal can be approached in two different ways. The traditional approach is based on the accepted value of 3-5ml/kg/hour, the primary problem with this approach is that it represents a very broad range of fluid rates and may result in fluid overload if not monitored closely. A second approach is based on the Holliday-Segar formula, which provides a more conservative rate of fluid administration. With this calculation there is administered 100ml/kg/day for the first 10kg of bodyweights, 50ml/kg/day for each kilogram from 11-20kg and then 25ml/kg/day for each kilogram of bodyweight >20kg. The use of hypotonic crystalloid solutions is the most appropriate as maintenance fluid because of their lower amount of sodium and chloride. Supplementation of potassium however can be necessary, certainly if the foal is not nursing. The addition of potassium chloride at 20 to 40 mEq/L to a hypotonic maintenance solution is a reasonable starting point.

Using the clinical perfusion indicators mentioned previously one can derive a rough estimate of the degree of clinical dehydration. This approach yields estimates of dehydration ranging from 5% tot > 10% and these values can be used when calculating the estimated fluid deficit.

Degree of dehydration	Skin tenting	CRT	Mucous membranes
<5%	1-3 sec	< 2 sec	Slightly tacky
5-10%	3-5 sec	2-3 sec	Tacky
>10%	> 5 sec	> 3 sec	Dry

Clinicopathologic testing can aid in refining the estimate of fluid deficit, with variables such as PCV, total plasma protein concentration, serum creatinine and lactate concentration all providing useful insights.

Parameter	Overhydrated	Ideal	Underhydrated
Heart rate	/	80-120	>140
Respiratory rate	Upward trend	<56	/
Hematocrit	20	35-45	>45
Total protein (g/L)	<30	50-80	>80
Urine Output (ml/kg/h)	>2	1-2	<0.5
Urine specific gravity	/	1.005-1.010	>1.012
Plasma lactate (mmol/L)	/	<2	>5 (neonate), > 2.5 (if >4 days old)
Peripheral edema	Obvious	May be seen in some foals	/
Central venous pressure (cm H ₂ O)	>8-12	3-8	0-5
BUN/Creatinine	/	normal	Increasing

Once a determination of the existing fluid deficit has been made, a **replacement fluid** plan can be formulated. Use of isotonic replacement fluid (LRS, Normosol-R and Plasmalyte A) is appropriate for this purpose. Rather than simply dividing up the calculated fluid deficit and administer it over a set period of time, it is more useful to administer boluses of replacement fluids at 20ml/kg over 10-30 minutes and then reassess the patient's status to determine whether further boluses are required. Care should be taken not to exceed 60ml/kg total dose, unless there are compelling clinical reasons that this is indicated, such as ongoing losses. If greater than 60 ml/kg of fluid replacement is required and the patient remains hypotensive, then they should be considered non-responsive to fluid therapy and the initiation of inotrope and/or vasopressor therapy should be considered.

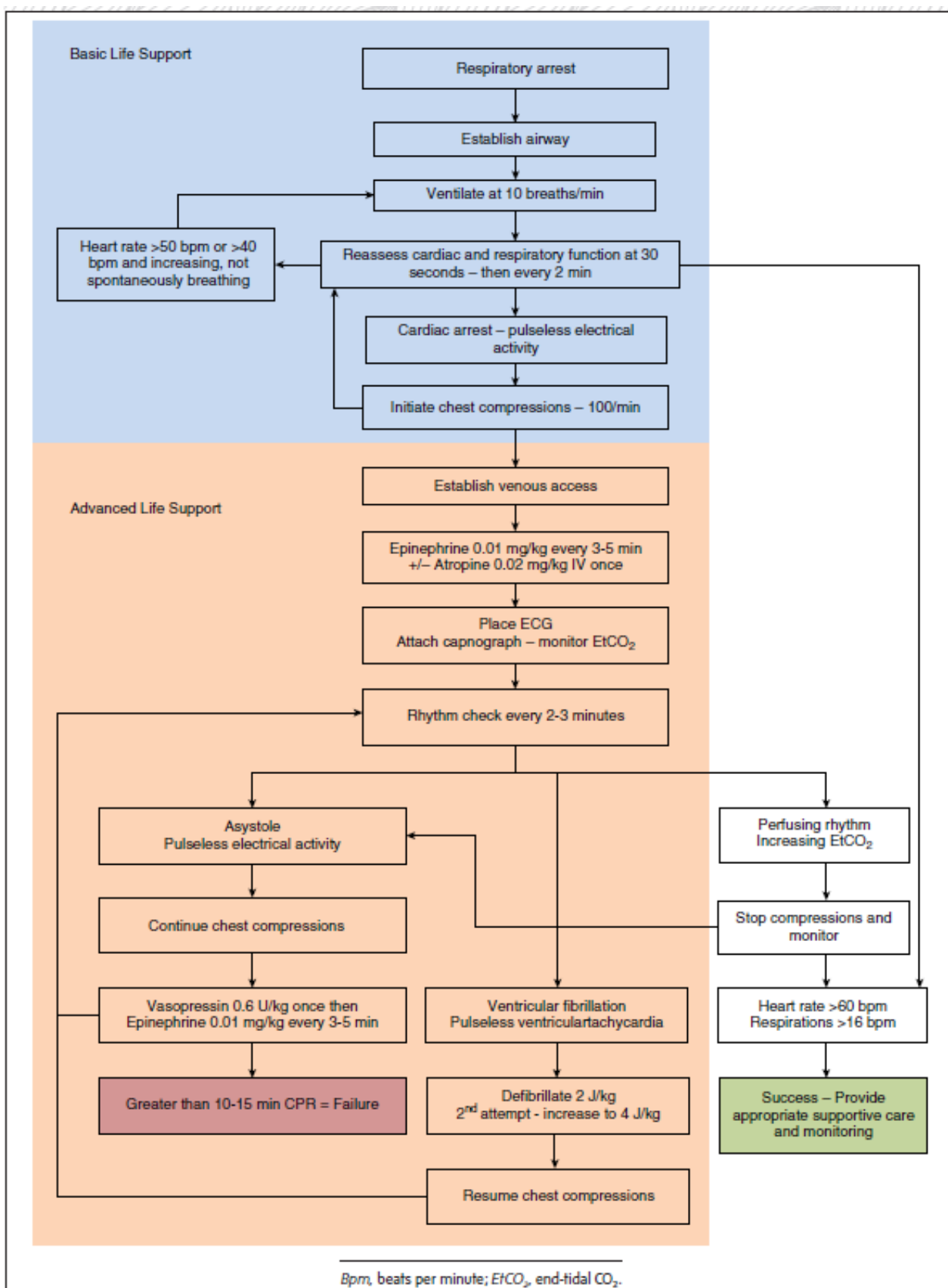
Monitoring of ongoing fluid therapy is very important and requires frequent assessment to ensure that the goals for fluid therapy are being achieved and to avoid the development of adverse outcomes such as fluid overload. Repeated assessment of the clinical indicators of hydration and perfusion status is readily performed and extremely valuable in monitoring fluid therapy.

Neonatal resuscitation

Cardio-pulmonary arrest in foals most commonly begins with respiratory arrest, which subsequently leads to cardiac arrest caused by asphyxia. Because of this the establishment of a patent airway and the provision of ventilator support is the initial priority in foals, rather than cardiac compressions.

The first challenge is in recognizing which foals require resuscitation, because early intervention before cardiac arrest is associated with a much higher likelihood of successful resuscitation, potentially as high as 50%. The clinical signs that may indicate the need for resuscitation include absence of breathing, irregular gasping, respiratory rate less than 10 breaths per minute, heart rate less than 40 beats per minute, irregular or absent muscle flaccidity, or lack of response to tactile stimulation. Other situations in which resuscitation may be required include primary lung disease, septic shock, hypovolemia, metabolic acidosis, hyperkalemia, hypoglycemia, vasovagal reflex and hypothermia.

If a foal fails to breath spontaneously and regularly then an airway needs to be established immediately and basic life support (BLS) should be implemented. The best approach to establish an airway is to pass a cuffed nasotracheal tube. Ventilation should be provided with a self-inflating valved manual resuscitation device at 10 breaths per minute. Excessive ventilation negatively affects cardiac return and coronary perfusion and has been associated with worsened outcome. As many as 90% of foals that require resuscitation will respond to ventilator support alone. If a heartbeat is absent or the rate is too low, then it is important to immediately initiate thoracic compressions. A rapid rate of 100 compressions per minute is advised, but compressions should be stopped every 2-3 minutes and should be resumed within 10 seconds. If the foal is not responding to Basic life support then more aggressive measures (Advanced life support) are indicated. These may include administration of pharmacologic agents and implementation of improved monitoring. Many drugs have been used empirically in foals resuscitation, but none has been specifically studied in the foal. The utility of many of these agents is debatable, either because they are directed toward primary cardiac dysfunction, which is rare in foals, or because their use in human cardiopulmonary resuscitation has been discontinued. The drug that is most likely to be used is epinephrine. Vasopressin has been used either in place of, or in combination with, epinephrine. Doxapram has been commonly used in foal resuscitation as a respiratory stimulant, but is contra-indicated because it does not reverse secondary apnea and has been shown to decrease cerebral blood flow and increase cerebral oxygen consumption.



Defibrillation

Defibrillation is indicated in cases of ventricular fibrillation and pulseless ventricular tachycardia. Access to appropriate equipment is often limited, however. The widespread availability of human automated electrical defibrillators may alter this situation, but at this time there are no published studies regarding their use in foals. When performing defibrillation the cardiac compressions and ventilation should continue until the moment of defibrillation and resumed immediately afterward. The initial charge should be 2 J/kg, which should be increased to 4 J/kg for subsequent attempts.

Monitoring Resuscitation

Patient status during resuscitation is extremely dynamic, requiring constant reassessment, and it can be difficult to monitor for return of spontaneous circulation and spontaneous respiration without interfering with the process of resuscitation itself. Following initiation of resuscitation efforts cardiac and respiratory function should be reassessed at 2- to 3-minute intervals unless the foal shows obvious signs of response. Monitoring via electrocardiography can be challenging, because electrical activity does not necessarily represent effective cardiac contractility, which is a phenomenon termed *pulseless electrical activity*. Respiratory efforts are much more readily observed and their effectiveness should be subjectively evaluated. One technique that can greatly facilitate monitoring during resuscitation is the monitoring of end-tidal CO₂ (EtCO₂), if capnography is available. During resuscitation a reasonable target for EtCO₂ is 10 mm Hg, because this indicates that an adequate degree of perfusion and ventilation is being achieved. If resuscitation is successful then a rapid increase in EtCO₂ toward the normal range will be observed, indicating that both perfusion and ventilation are improving. A decrease in EtCO₂ during resuscitation indicates inadequate ventilation and perfusion, requiring reevaluation of how resuscitation is being performed. If no response is detected after 10 to 15 minutes of resuscitation it is extremely unlikely that the patient will respond with further efforts.

Postresuscitation Support

Following successful resuscitation the patient should be considered at high risk because of the presence of any primary, initiating diseases and the likelihood of secondary hypoxic injury. Appropriate medical care and monitoring are critical during this period of time. Foals should receive intranasal insufflation of humidified oxygen at 5 to 10 L/min until they have been demonstrated to be stable with adequate cardiopulmonary function. Fluid therapy will likely be of benefit in ensuring normovolemia and supporting cardiovascular function. Care should be taken to avoid overhydration, because these patients may be at risk of pulmonary edema. Pressor and inotrope therapy may be indicated if cardiovascular function is inadequate. Glucose support is important, especially in neonates, but care should be taken to avoid hyperglycemia. If resuscitation occurred in the field then serious consideration should be given to immediately referring the foal to a facility equipped to provide intensive care.

15.45 – 16.30

Sepsis and perinatal infections in foals

(A. Dufourni)

Sepsis and perinatal infections in foals

Neonatal foals are immunocompetent at birth but are immunologically naïve. They have no memory response associated with adaptive immunity and have minimal amounts of immunoglobulins. Therefore, absorption of hyperimmune colostrum is required to gain immediate protection against various pathogens within the environment. Failure of passive transfer of maternal antibodies (FPT) can occur when insufficient quantity or quality of colostrum is consumed. Inadequate absorption may be caused by maternal (agalactia, inadequate quantity or quality of colostrum, pre-partum lactation, rejection of the foal, illness of the mare, twin pregnancy, abnormal behavior or maternal death during parturition) or neonatal factors (pre- or dysmaturity, increased use due to septicemia or illness, musculoskeletal, neurologic or gastrointestinal disorders). The concentration of IgG absorbed by the foal can be measured quantitatively or semiquantitatively in serum, plasma or whole blood by protein electrophoresis, immunoglobulin determination, glutaraldehyde test or a commercial ELISA SNAP FOAL IgG Test Kit® (IDEXX Laboratories). IgG concentrations of >800 mg/dl indicate adequate passive transfer of immunoglobulins. If lower amounts of IgG immunoglobulins are detected, foals should receive hyperimmune equine plasma or colostrum. Good-quality colostrum or equine plasma can be administered orally if foals are younger than 12 hours of age. Colostrum should be administered into several smaller (300–500 ml) oral increments within the first 12 hours of life. The ability of the equine small intestine to absorb colostrum by pinocytosis decreases within 6-12 hours after birth and is greatly reduced to absent within 12 -18 hours. From this point, intravenous administration of hyperimmune equine plasma is indicated. Control of IgG concentration is indicated until sufficient amounts of protective immunoglobulins are reached as the risk of infection or death increases proportionally with decreasing IgG concentrations. In foals with failure of passive transfer of immunity, the incidence of neonatal septicemia and related complications increases significantly. To assess the inflammatory state of the neonate, inflammatory acute phase proteins, such as SAA or fibrinogen can be used and act as a biomarker for bacterial infection in neonatal foals. Although cutoff values >100 mg/l are highly suggestive of infection, low SAA concentrations do not rule out the possibility of bacterial septicemia.

Equine neonatal septicemia is a systemic disease process caused by the presence of pathogenic microorganisms and/or their toxins in the foal's blood. These circulating endotoxins or microorganisms cause a systemic inflammatory response (SIRS) which can lead to severe hypotension, tissue hypoperfusion and multiple organ dysfunction. Although bacterial infection is responsible for the initiation, the inflammatory response itself is responsible for the production of endogenous inflammatory mediators, which results in an increased production of vasoactive mediators and an alteration of the vascular homeostasis. The earliest systemic effect is pulmonary vasoconstriction which leads to pulmonary hypertension. This pulmonary hypertension is followed by systemic hypotension caused by a decreased arterial tone resulting in a decreased left ventricular afterload and venous vasodilatation which decreases the venous return and the right ventricular preload. The resulting hyperdynamic shock requires an increased heart rate and cardiac output to maintain tissue perfusion. However, this compensatory response is impaired by the reduction in left ventricular preload from a decreased peripheral vascular resistance and decreased cardiac contractility. Additionally, arteriolar

vasoconstriction, vascular neutrophil adherence or fibrin and platelet aggregation cause changes within the microvasculature, which potentiate the decreased tissue perfusion. Activation of the extrinsic pathway of coagulation, impairment of fibrinolysis and inhibition of coagulation result in a consumptive coagulopathy leading to disseminated intravascular coagulation (DIC). Leakage of intravascular fluid into the interstitial space further contributes to hypotension and hypovolemia and causes tissue edema. Finally, the resulting cardiovascular shock leads to multiple organ failure (MOD) characterized by cardiovascular, pulmonary, renal, gastrointestinal, central nervous and hepatic dysfunction.

This important neonatal disease can be acquired in utero or can be caused by bacterial translocation from the respiratory or gastrointestinal tract, umbilical cord or wounds after birth. Risk factors for neonatal septicemia include placentitis, pre-parturition vulvar discharge, dystocia, maternal illness, prematurity or delayed parturition, premature placental separation, induced parturition, partial or complete failure of passive transfer, poor hygiene, improper umbilical care, prolonged transport of the mare and presence of localized disease in the foal. Clinical signs of neonatal septicemia are vague and nonspecific and may include depression, lethargy, partial or complete absence of nursing behavior, tachycardia, tachypnea, hypotension, hypo- or hyperthermia, abnormal mucous membranes color with prolonged capillary refill time, dark red or injected mucous membranes; petechiation of mucous membranes, skin or inner pinnae, inability to stand and weakness. Additional clinical signs of localized infection, such as omphalitis, patent urachus, diarrhea, joint effusion with or without lameness or osteomyelitis, physeal distention, respiratory distress, uveitis or seizures may be present. Clinicopathological evaluation of the septicemic foal can reveal low white blood cell ($< 6.9 \times 10^3$ cells/ μ l), neutrophil and lymphocyte counts, higher band neutrophil (> 5 -10%) and monocyte counts, azotemia, hypoglycemia (< 50 mg/dl), acidosis (metabolic, respiratory or mixed), hypoxemia ($\text{paO}_2 < 60$ mmHg), hypercapnia ($\text{paCO}_2 > 50$ mmHg) or increased venous blood lactate concentrations (> 5 mmol/l).

Rapid identification of a septic neonate and rapid implementation of appropriate treatment are determinative for survival and prognosis. The most appropriate diagnostic tool for ante mortem diagnosis of septicemia remains blood culture performed at presentation, ideally before administration of antimicrobial drugs. Due to false negative results in up to 37% of fatal septicemic cases, repeated blood cultures and multiple susceptibility testing are recommended to maximize diagnostic sensitivity and follow up of antimicrobial susceptibility over time. Early administration of appropriate antimicrobials is essential for survival of the septicemic neonate. Human consensus statements recommend intravenous antimicrobial treatment within the first hour of recognition of septicemia to decrease the odds of morbidity and mortality. Historically gram-positive organisms were most commonly associated with neonatal infections, but over the past years the most common isolated bacteria have been gram-negative organisms, especially Enterobacteriaceae. Gram-positive organisms appear to occur often in mixed infections. Aggressive, early antimicrobial therapy with broad-spectrum coverage is indicated in these patients. Current recommendations state that the combination of a beta-lactam antibiotics (penicillin or ampicillin) in combination with an aminoglycoside (typically amikacin) should be used as initial approach. Monotherapy with a third- or fourth generation cephalosporin (ceftiofur) may be an alternative

to the combination therapy, especially in hypoperfused patients, but may not provide a full gram-positive coverage. Note that the most common bacterial isolates and antimicrobial susceptibility patterns may vary depending on geographical location and study population.

M. J. P. Theelen et al. Temporal trends in prevalence of bacteria isolated from septic foals

TABLE 2: Temporal trends in prevalence of bacteria causing sepsis in foals admitted to the VMTH, UC Davis, USA, 1979–2010

Bacterial species	1979–1990 (n = 328)		1991–1997 (n = 415)		1998–2010 (n = 348)	
	No. isolates	Percentage of total isolates (%)	No. isolates	Percentage of total isolates (%)	No. isolates	Percentage of total isolates (%)
Gram-negative bacteria*	243	74.1	300	72.3	223	64.1
Enterobacteriaceae*	161	49.1	218	52.5	144	41.4
Escherichia coli	90	27.4	145	34.9	78	22.4
Klebsiella spp.*	34	10.4	26	6.3	20	5.7
Enterobacter spp.	13	4.0	18	4.3	11	3.2
Salmonella spp.	12	3.7	8	1.9	12	3.4
Proteus spp.	7	2.1	8	1.9	9	2.6
Actinobacillus spp.	53	16.2	56	13.5	43	12.4
Pseudomonas spp.	13	4.0	4	1.0	10	2.9
Other Gram-negative isolates	16	4.9	22	5.3	26	7.5
Gram-positive bacteria*	85	25.9	115	27.7	125	35.9
Streptococcus spp.	47	14.3	63	15.2	51	14.7
β-haemolytic streptococci	29	8.8	37	8.9	37	10.6
Enterococcus spp.*	18	5.5	19	4.6	42	12.1
Staphylococcus spp.	14	4.3	22	5.3	22	6.3
Coagulase positive staphylococci	8	2.4	11	2.7	12	3.4
Coagulase negative staphylococci	6	1.8	10	2.4	8	2.3
Other Gram-positive isolates	6	1.8	11	2.7	10	2.9

(Theelen M.J.P et al. (2014). Temporal trends in prevalence of bacteria isolated from foals with sepsis: 1979–2010. Equine Vet. J. 46, 169-173.)

M.J.P. Theelen et al./The Veterinary Journal 243 (2019) 74–76

Table 1
Cumulative susceptibility at 'foal level' of bacteria isolated from foals with sepsis at hospital admission (UC Davis, USA) between 1 January 1990 and 31 December 2015.

Antimicrobial drug (combination)	Number of foals	Percentage of foals from which all isolates were susceptible	95% confidence interval
Amikacin	213	63.4%	56.5–69.9
Amikacin + penicillin	210	88.6%	83.5–92.5
Amikacin + ampicillin	213	91.5%	87.0–94.9
Gentamicin	213	62.0%	55.1–68.5
Gentamicin + penicillin	211	82.0%	76.1–86.9
Gentamicin + ampicillin	213	83.6%	77.9–88.3
Ceftiofur	211	86.3%	80.9–90.6
Ceftiofur + amikacin	211	89.6%	84.6–93.4
Ceftiofur + ampicillin	211	89.7%	84.5–93.6
Chloramphenicol	207	81.6%	75.7–86.7
Enrofloxacin	211	82.9%	77.2–87.8
Imipenem	175	92.6%	87.6–96.0
Trimethoprim/sulfa-methoxazole	213	59.6%	52.7–66.3

(Theelen M.J.P et al. (2019). Initial antimicrobial treatment of foals with sepsis: Does our choices make a difference? Vet. J 243, 74 -76.)

Additional treatment of septicemic foals requires constant monitoring and nursing care. Fluid therapy consists of 20 ml/kg boluses of polyionic fluid without glucose over 10-30 minutes, followed by maintenance fluid therapy. Inotropes (dobutamine) and vasopressors (norepinephrine, vasopressin) are necessary in case of persistent hypotension (<65 mmHg) refractory to fluid and /or colloid support. Fluid-refractory and vasopressor-resistant hypotensive patients may benefit of physiologic dosages of hydrocortisone (1-4 mg/kg divided into 4-6 boluses per day). Intranasal oxygen (5-10 L/min) is also indicated. Respiratory stimulants (caffeine or doxapram) are indicated in hypopneic foals and

mechanical ventilation may be necessary if arterial pCO₂ exceeds 70 mmHg. Maintenance of physiologic levels of glycaemia is essential for survival and hypo- (<50 mg/dl) and hyperglycemia (>180 mg/dl) should be avoided. Due to insulin resistance, many foals require initial insulin support by CRI-infusion. Sucralfate is a reasonable choice of gastroprotectant therapy as proton pump inhibitors are not indicated until the age of 4 weeks due to increased risk of nosocomial infections. Urinary catheterization is indicated to prevent bladder rupture in recumbent foals. Parenteral (glucose, amino acids, lipids) and enteral support (mares or artificial milk by indwelling nasogastric tube) is often needed. Prognosis remains reserved due to risk of severe complications (see perinatal infections). Recently, several sepsis scoring systems have been developed to predict severity of septicemia and survival in foals, but clinical judgement still remains highly important. An estimation of survival can be achieved by using the Dembek's foal survival score (FSS): a score of ≥ 4 predicts survival; a score of < 4 predicts non-survival. Equine neonatal septicemia can be associated with several important perinatal infections which are discussed in the following section.

Septic encephalopathy (SAE) or sepsis-associated brain dysfunction is caused by disturbances of neurotransmission, derangements of neuronal calcium homeostasis, direct neuronal cell injury as well as mitochondrial and endothelial dysfunction. Clinical signs include abnormal behavior, alteration of sleep state, disturbances of consciousness and coma. Clinical signs resemble strongly to perinatal asphyxia syndrome (PAS) or hypoxic ischemic encephalopathy (HIE, syn.: dummy foals) which are non-infectious causes of neonatal brain dysfunction caused by cerebral hypoxia and ischemia as well as a dysregulation of neurosteroid concentrations. Sepsis associated bacteria, such as *Escherichia coli*, *Actinobacillus* spp, *Klebsiella* spp, *Streptococcus* spp or *Salmonella* spp. may also cause a bacterial meningoencephalitis. Beside the earlier mentioned neurological alterations, clinical signs of bacterial meningitis include abnormal pupillary light responses, hyperesthesia, fever, nystagmus and blindness. Definitive diagnosis of a bacterial meningoencephalitis requires CSF analysis (TNC > 7 cells/ μ l, TP > 120 mg/dl) and shows mostly neutrophilic pleocytosis. Treatment consist of anti-inflammatory and antimicrobial therapy able to penetrate the blood brain barrier. Commonly used antimicrobial drugs such as beta-lactams, aminoglycosides and ceftiofur are of little value due to limited penetration to the CNS.

Umbilical disease is common in equine neonates and include persistent urachus, patent urachus, hematoma, herniation or umbilical infection. Umbilical infection may be limited to a local cellulitis or infection of the interior or exterior umbilical structures. Diagnosis can be made by ultrasound of the umbilical entities (1 vein, urachus, 2 arteries), bacterial culture (swab or aspiration) and blood culture. Umbilical infection may be caused by hematogenous spread of septicemic organisms or by local invasion of environmental bacteria. Clinical signs of omphalitis/omphalophlebitis include fever, a swollen and warm umbilicus which may be painful on palpation or reveal purulent discharge. An infected umbilicus can be a portal for environmental pathogens (mostly Enterobacteriaceae), which can then lead to secondary infections such as polyarthritis, physisitis or osteomyelitis. Monitoring of the white blood cell count and inflammatory proteins as well as ultrasonographic follow up are indicated to evaluate treatment's efficacy. Systemic broad spectrum antimicrobial treatment and local disinfection resolves infection in many cases. Refractory cases require surgery.

Pneumonia in neonatal foals is mostly the result of meconium aspiration during delivery, post-partum aspiration pneumonia of milk, bacterial infection due to septicemia or infection by inhalation. Viral respiratory infections are uncommon in neonatal foals and occur more commonly in older foals, but infections caused by EHV-1, EHV-4, EIV, EAV or EAdV are reported in neonates. Especially EHV-1 infections may be present in weak or premature foals with respiratory insufficiency. Fungal pneumonia is very rare in neonatal foals, but systemic candidiasis may cause clinical signs similar to bacterial septicemia. Most common bacterial isolates in foals suffering from pneumonia are *Escherichia coli*, *Klebsiella* spp, *Actinobacillus* spp, *Pasteurella* spp, *Streptococcus* spp, *Salmonella* spp., *Streptococcus* spp., *Enterococcus* spp. and *Staphylococcus* spp.. Aggressive and/or extensive need for ventilatory support may predispose for bacterial colonization of the lower airways. Diagnosis is made by blood culture and culture of transtracheal aspiration. Treatment consists of support of the ventilatory function, correction of hypoxemia, anti-inflammatory and antimicrobial drugs. Due to possible mixed infections, broad-spectrum therapy with sufficient lung penetration (3rd generation cephalosporin) is indicated as initial therapeutic approach.

Diarrhea or enterocolitis is a common problem in foals and can be non-infectious or infectious in origin. The most common origin of infectious diarrhea is a rotavirus infection (20-77%) and affected foals age ranges typically from 5 to 35 days. Common bacterial agents involved in infectious diarrhea are commonly *Clostridium difficile* and *Clostridium perfringens* and may be characterized by transient hemorrhagic diarrhea. Other bacterial isolates include *Salmonella* spp, *Escherichia coli*, *Enterococcus* spp, *Aeromonas* spp and *Bacteroides fragilis*. As diarrhea is a common clinical finding in septicemic foals, bacterial involvement may be present even as a non-primary enteric pathogen. Foals with diarrhea can suffer from metabolic acidosis (lactic acidosis and enteric loss of sodium bicarbonate) and prerenal azotemia. They are often hyponatremic and hypochloremic. Treatment is supportive and symptomatic. It implements parenteral nutrition and a minimal enteral nutrition approach. Balanced electrolyte replacement solutions, broad-spectrum antimicrobials, lactase enzymes, probiotics and enterally administered di-tri-octahedral smectite adsorbents are commonly used therapeutics. *Cryptosporidium parvum* or *Strongyloides westeri* can be parasitic causes of diarrhea in neonatal foals, but they are often self-limiting or only relevant in case of very high exposure.

Septic arthritis, polysynovitis, physitis or osteomyelitis result from hematogeneous spread of septicemic organisms to the synovial or bone structures. Depending on the site of infection, subdivision into type S (synovial membrane), type E (epiphyseal subchondral bone) or type P (metaphyseal side of physis) infection can be made. Type T infections describe premature infection of the cuboidal bones of tarsi and carpi. Foals younger than 3 weeks of age have mostly several sites of infection, while foals older than 3 weeks have mostly only one affected joint or physis. The most prevalent bacterial isolates are Enterobacteriaceae such as *Escherichia coli*, *Salmonella* spp., *Actinobacillus equuli* spp. and *Klebsiella* spp., but also *Staphylococcus* spp., *Streptococcus* spp. or *Rhodococcus equi* can be involved. Serosanguinous, cloudy to opaque and non-viscous synovial fluid with a TNC count exceeding 10 000 - 30 000 leucocytes/ μ l with more than 80% neutrophils and a TP > 4 g/dl is highly suggestive for synovial infection. Radiographs, CT- or MRI-scans reveal information about bone changes and osteomyelitic processes. Ultrasonography provides information about periarticular or soft tissue structure involvement.

Therapeutic options are systemic or local antimicrobial treatment, intrathecal catheterization, regional limb perfusion by intravenous or intraosseous injection or arthroscopic debridement and lavage. Prognosis is generally fair to good if no other significant comorbidities or multidrug resistance are present. However, affected foals are less likely to reach athletic performance, or attain it at later age, than sibling controls.

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Dufourni Alexander, DVM

Department of Large Animal Internal Medicine - Ghent University

16.30 – 17.30

Fluid therapy and sepsis in ruminants

(B. Pardon)

Fluid therapy and sepsis in ruminants

B. Pardon

Department of Large Animal Internal Medicine, Faculty of Veterinary Medicine, Ghent University, Salisburylaan 133, 9820 Merelbeke

Because they are prey animals, ruminant newborns can quickly adjust to their environments, stand and join the herd. Also, these species show robustness, hiding signs of illness as long as possible to prevent being targeted by predators. Whereas the robustness would actually provide calves with better survival chances, in modern farming situations their nature to hide clinical signs often results in a too late disease detection by the producers and poorer prognosis. Therefore, bovine veterinarians are frequently confronted with the critically ill calf. They need to deal with these patients in field situations, without access to advanced measurement devices and a legally limited pharmaceutical options.

Key features of the critically ill patient are severe respiratory, cardiovascular or neurological derangement, often in combination. The different types of shock can be part of the presentation. Especially newborns and calves aged < 3 weeks old are presented in a critically ill state. In newborn calves, metabolic and respiratory acidosis (dystocia and maladaptation to extrauterine life), neonatal respiratory distress syndrome, congenital heart defects, hemorrhage and septicemia are among the most common differential diagnoses. In the first three weeks, enteritis (Enterotoxigenic *Escherichia coli*, rotavirus, coronavirus and *Cryptosporidium parvum*) is the leading disease. As a consequence, animals dehydrate, develop acidosis, ion disturbances, malabsorption and hypoglycemia. If this situation of negative energy balance and dehydration persists, renal failure, a cachectic state and negative effects on innate immunity develop. Very often, calves with neonatal diarrhea, either develop pneumonia at the same time or are more susceptible to pneumonia in later life (Pardon, 2013). Older studies show that of all calves with diarrhea, both critically ill or not, about 30% is septicemic (Fecteau et al., 1997a). Calves are born almost agammaglobulinemic and need to consume colostrum to assure adequate passive transfer of immunity. However, failure of passive transfer, is very common in cattle farming (20-40% of the animals), and one of the main risk factors for septicemia (Lofstedt et al., 1999). In contrast to other species, calves are prone to the development of D-lactic acidosis, due to dysbiosis (Lorenz, 2009). Signs of this condition include severe depression, tachypnea, abnormal posture and an instable gait. A reduced or incomplete palpebral reflex was identified as a reliable clinical indicator for the degree of D-lactic acidosis in calves (Trefz et al., 2012). Therefore, D-lactic acidosis can be life-threatening condition as such, and an important differential diagnosis for a septicemic calf.

This lecture aims at giving practitioners a state of the art on diagnosis and treatment of sepsis in calves. A tone of 'sceptis about sepsis' will never be far away, given the current possibilities for food animals in practice. A paper on this talk with full scientific reference is available elsewhere (Pardon et al., 2018).

To successfully treat sepsis, early administration of appropriate antimicrobials is crucial. In veterinary practice the critically important fluoroquinolones and cephalosporins are popular

molecules for this indication, because of their bactericidal effects, broad-spectrum activity and relatively low resistance levels. In different European countries legislation has placed the use of critically important antimicrobials under strict terms. In Belgium for example, these molecules can only be used in food animals when (1) the patient is examined by a veterinarian, (2) the disease has a bacterial etiology, (3) after adequate sampling and bacteriological culture in an accredited laboratory, (4) identification of the bacterial strain which likely caused the infection and (5) comparison of the strains susceptibility with at least 7 other not critically important antimicrobials, belonging to at least 5 different antimicrobial classes. The legislation allows the following exceptions in which critically important antimicrobials can be used without previous laboratory confirmation: (1) if no laboratory result is reached or sampling is impossible (in this case the veterinarian can use the molecules based on recent scientific data); (2) if laboratory results fulfilling the first 5 requirements above are available for the same group of animals in the same farm (valid for 6 months in veal calves, and 1 year for other cattle operations) and finally (3) for ‘urgency’ reasons to save the life of a single animal. In the latter case the veterinarian needs to treat the patient him/herself, after a clinical examination and obligatory sampling and culturing. As soon as an antimicrobial susceptibility test result is reached, re-assessment of antimicrobial therapy and de-escalation to a non-critically important antimicrobial is obliged, whenever possible. In Belgium and the Netherlands, formularies to advice veterinarians on their antimicrobial choice are available. Given the different advices currently provided for the different species, it is clear that merging the priority to minimize fluoroquinolone and cephalosporin use with the desire to work evidenced based is particularly difficult for sepsis.

Key information is that approximately 30% of diarrheic calves is septicemic, with no further insights on what proportion has sepsis, severe sepsis or septic shock (Fecteau et al., 1997a). To predict sepsis, largely three published models/scoring systems for calves are available, with reported sensitivity and specificity ranging between 39% and 77%, and 90.6% and 75%, respectively (Fecteau et al., 1997b and Lofstedt et al., 1999). However, evaluation of these models on a new dataset of critically ill calves, showed very poor sensitivity and specificity. Most laboratory parameters can improve the diagnostic accuracy of these models only with some percentages (Lofstedt et al., 1999). As in humans, procalcitonin is the most promising biomarker for sepsis, and recently a cut off of >68 pg/mL was suggested (Sensitivity= 77%; Specificity= 79%) (Bonelli et al., 2018). Cow-side tests or faster laboratory turnaround times are required to make this test available for practice. The world health organization approach for antimicrobial decision making will be applied to the case of sepsis in calves. In contrast to humans, sepsis in calves is predominantly of gram negative origin, with mainly *Escherichia coli* and to a lesser extend *Salmonella spp.* (Fecteau et al., 2009). The gastro-intestinal tract and umbilicus are the most likely source of infection in calves, although no hard evidence is available. Recommended samples for etiological diagnosis are sterile taken blood cultures (enriched environment, eg. Bactec systems). A single, large volume sample is recommended. In some cases of outbreaks of septicemic bacteria such as *Histophilus somni*, *Mycoplasma bovis* or *Salmonella spp.* a respiratory or faecal sample might be sufficient. MALDI-TOF MS offers promising technology to reduce the turn-around time between sampling and availability of the antibiogram. For example, etiological bacteria can be detected from blood cultures within 3-6 hours after sampling (Morgenthaler and Kostrzewa, 2015). An antibiogram for bovine pathogens can be available as quickly as within 3 hours after culture, with better accuracy than the disc diffusion antibiogram (Van Driessche et al., 2018). *E. coli* and *Salmonella spp.* are both

renowned for their accumulation of resistance genes. In our clinic, *E. coli* isolated from sepsis cases show high levels of resistance to sulfonamides-trimethoprim, oxytetracycline, doxycycline, and amoxicillin, whereas recent *Salmonella spp.* isolates showed little resistance. Fast (< 1h) administration of a bactericidal, broad spectrum antimicrobial remains the cornerstone to survive sepsis in every species. Rapid administration of crystalloids at 30 mL/kg body weight is recommended for humans (Dellinger et al., 2017). A major difference with other species is D-lactic acidosis in calves, which requires intensive treatment with hypertonic bicarbonate solutions. Corticosteroids did not show benefits for survival, not in humans nor calves (Plessers et al., 2012, Aronoff et al., 2012). In contrast to humans, in calves ketoprofen significantly reduced the rise in temperature and respiratory rate in an endotoxin challenge model (Plessers et al., 2016). Prognosis of sepsis in calves is poor with mortality rates ranging between 46.8% and 77.1% in the handful of studies available (Fecteau et al., 1997b, Trefz et al., 2017). In humans, the disastrous effect of the use of an inappropriate antimicrobial (antimicrobial for which the bacteria are resistant) as first intention treatment on survival (-42%) has been clearly documented (Kumar et al., 2009).

In conclusion, a lot needs to be done before bovine veterinarians will have reliable diagnostic tests to identify sepsis patients in the field. The inverse interest of on the one hand working evidence based and maximizing survival chances of the animal and on the other safeguarding products for human medicine, will remain a hot topic in the years to come. The least what practitioners can do is attempting to work as much evidence based as possible, limiting the use of critically important antimicrobials to selected case, underbuilding their decision with a laboratory diagnosis.

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